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AETIOLOGY, DIAGNOSIS, AND TREATMENT OF EARLY VITAMIN-DEFICIENCY STATES

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Vitamins are chemically and structurally heterogeneous organic compounds, and their functions—so far as they are known—differ even more. They are produced either in negligible amounts or not at all in the human body, do not furnish energy, and are not utilized as building units for the structure of the organism; they are able to perform their complicated functions in the transformation of energy and for the regulation of metabolism in minute quantities.

Following the spectacular advance in vitamin research, clinical medicine has not been able to keep pace with the laboratory. For the same reason we know now a larger number of different vitamins than identified human deficiency syndromes. Naturally occurring avitaminosis is mostly due to multiple deficiencies, and therefore controlled animal experiments with deprivation of one single vitamin cannot easily be translated to human beings.

Aetiology of Vitamin-deficiency States

The causes of vitamin-deficiency states are either primary or conditioned.

Primary Deficiency.—Nutritional deficiency states of the tissues may be caused solely by inadequate diet, and this is termed primary deficiency. Primary deficiency states are comparatively rare in this country at present. They are, however, occasionally seen in single old people who are either unable to collect their food or to cook it properly, or in persons with self-imposed restriction of essential food intake (Leitner, 1948a). By "dietary inadequacy" is meant the failure to ingest an essential nutritional factor in sufficient amounts to meet the existing body requirements. "Nutritional inadequacy" means not only the failure to ingest (i.e., dietary inadequacy) but failure to absorb and to utilize essential nutritional factors in sufficient amounts to meet these requirements. "Nutritional failure" occurs when essential nutritional factors fail to reach the tissues and the protective mechanisms of the body are unable to compensate the malnutrition. At that point symptoms begin to appear. The factors responsible for inadequate intake (primary deficiency) are poverty, ignorance, improper cooking and preparation of food, and self-imposed restriction of essential food (faddiness, eccentricity, anxiety).

Secondary or Conditioned Deficiency.—Nutritional deficiency states occurring on adequate dietary intake are known as secondary or conditioned deficiency. The importance of conditioning factors as a cause of deficiency states has not always been sufficiently recognized. Even when gross manifestations of deficiency disease caused by conditioning factors are recognized the findings may lead to one of two errors (Jolliffe, 1942): (1) to consider the lesion a manifestation of the original or conditioning disease unrelated to tissue depletion (e.g., to attribute polyneuropathy to pyloric stenosis); (2) after recognizing the nutritional basis of the secondary manifestation, to attribute the original disease solely to nutritional deficiency (e.g., in the case of a middle-aged edentulous woman to ascribe the symptoms only to malnutrition, disregarding the loss of teeth, the often associated dysphagia, achlorhydria, etc.). The first error ignores the existence of deficiency disease, the second ascribes most deviations from normal health to malnutrition only.

These conditioning factors are: (*a*) interference with ingestion; (*b*) interference with absorption; (*c*) interference with utilization; (*d*) increased body requirements; (*e*) increased excretion; and (*f*) increased destruction.

Interference with Ingestion

The inclusion of this as a conditioning factor is warranted owing to the frequency with which abnormal conditions and disease may interfere with adequate food intake. For example, in hospitals the food intake is often calculated from the meals served to the patients. It is common knowledge that even convalescent hospital patients consume only a part of the meals as served (DuBois and Chambers, 1942). Our experts similarly calculate an adequate food intake for the population in this country. It is, however, very probable that the monotony of our diet for the last six to seven years, the lack of choice, and the fact that the population's very limited variety in food depends more on the chance of the food available on the world market than on their taste may be considered as a conditioning factor. For a considerable part of the population the relatively low protein and fat and high carbohydrate proportion of our food might be a further aggravating factor.

Gastro-intestinal and psychiatric disorders, causing anorexia, nausea, and vomiting, are clear examples of conditioning; alcohol in place of other food, causing anorexia and chronic gastritis and reducing thiamin intake, also provokes a change from a previously satisfactory diet to something like dry toast, highly seasoned food, coffee, or spirits, which may lead again to any of the deficiency diseases.

Diets prescribed with prolonged restriction of certain essential food factors are occasionally responsible for deficiency states—e.g., in peptic ulcers, obesity, colitis, food allergy, and nephritis. Slimming diets are especially harmful, though their low calorie content gives some measure of protection for a limited time. Even well-planned reducing diets are usually short of B vitamins, and it is advisable to supplement them with brewer's yeast and vitamin A concentrate.

TABLE I.—*Factors Interfering with Ingestion*

Anorexia:	Due to alcohol, operations, debilitating or infectious diseases, congestive heart failure, pregnancy, thiamin deficiency.
Gastro-intestinal disorders:	Gastro-enteritis, vomiting, peptic ulcer, gall-bladder disease, obstructive lesions of the gastro-intestinal tract.
Neuro-psychiatric disorders:	Psychosis, neurosis, migraine, anorexia nervosa, neurological disorders interfering with food intake.
Unsatisfactory denture, loss of teeth.	
Therapeutic restriction of essential foods:	Peptic ulcer, obesity, nephritis, allergy, occasionally gall-bladder disease and diabetes.
Monotony and lack of variation in the diet:	Disproportion in the protein, fat, and carbohydrate ratio.

Interference with Absorption

Anatomical, chemical, and physiological changes (Beams *et al.*, 1941) may all interfere with the absorption from the intestinal tract. The reduction of the absorbing surface, hypermotility of the gastro-intestinal tract, and absorbents and lubricants introduced perorally may all be instrumental. In diarrhoeic conditions the reduction of the absorbing surface and

the hypermotility with the rapid passage are causal factors. The clinical importance of diarrhoea in producing pellagra, sprue, riboflavin deficiency, hypocalcaemia, and vitamin A and D deficiency is well known. In the sprue syndrome the hypermotility seems to be reduced by improvement of phosphorylation (Leitner, 1942), by an adequate supply of the B complex in the form of crude liver extract, or even quicker by synthetic folic acid (Spies *et al.*, 1946; Manson-Bahr and Clarke, 1946).

Achlorhydria may interfere with the absorption of ascorbic acid (Alt *et al.*, 1939) and of thiamin (Melnick *et al.*, 1941). In unexplained malnutrition, especially in patients over 40, achlorhydria should always be suspected.

Bile salts play an important part in the absorption of fat and of the fat-soluble vitamins, especially that of vitamin A (Breese and McCoord, 1939) and natural vitamin K (Snell, 1939). The habitual taking of liquid paraffin for bowel regulation also interferes with the absorption of vitamin A (Andersen, 1939) and vitamin K (Elliott *et al.*, 1940). Aluminium hydroxide and kaolin may absorb the water-soluble vitamins from the gut (Bicknell and Prescott, 1946). Resection, short-circuiting operations, and fistulas of the gastro-intestinal tract have long been known to produce macrocytic anaemia and the sprue syndrome (Bennett and Hardwick, 1940). Peripheral neuritis due to interference with absorption in cases of pyloric stenosis, dysphagia, cardiospasm, and neoplasms of the gastro-intestinal tract may respond to parenteral treatment with thiamin (Laurent and Sinclair, 1938).

TABLE II.—*Factors Interfering with Absorption*

Achlorhydria.
Vitamin deficiency (sprue syndrome).
Gastro-intestinal disorders:
  Hypermotility, reduction of absorbing surfaces, loss of mucosal integrity (carcinoma of stomach, intestinal tuberculosis, gastro-intestinal fistulae).
Biliary disorders, especially obstructive jaundice.
Therapeutic measures:
  Liquid paraffin, colloidal absorbents, gastro-intestinal resections, short-circuiting operations, severe catharsis.

Interference with Utilization

The evidence for this is mainly circumstantial, as direct experimental verification is extremely difficult. Provided that the intake is adequate, it is imperative to exclude interference with absorption, increased destruction and excretion, as well as abnormal requirements before defective utilization may be concluded. Carotene has to be converted into vitamin A; thiamin phosphorylated into cocarboxylase; nicotinic acid into coenzymes I and II, etc. These changes may occur in different tissues, but at present most evidence points to the liver as being the main organ for these processes (Moore, 1931; Sydenstricker, 1941), although it was recently suggested that carotene might be converted into vitamin A in the intestine (Glover *et al.*, 1947). In the case of liver dysfunction not only the conversion but also the storage and release of these substances is interfered with. In this way the body becomes dependent on the very variable daily intake, and as storage of the excess is also impaired a deficiency is bound to occur sooner or later.

Vitamin-A deficiency has been established in chronic liver diseases (Haig and Patek, 1942), obstructive jaundice (Stewart and Rourke, 1941), and hypothyroidism (Wohl and Feldman, 1939). Similarly in certain skin conditions, such as Darier's disease, Devergie's disease, and ichthyosis, in which low plasma vitamin-A values were repeatedly observed, impaired liver function could be demonstrated (Leitner, 1946a; Leitner and Moore, 1946). The low plasma vitamin-A levels found in patients with cancer of the gastro-intestinal tract have been attributed to failure in utilization due to hepatic dysfunction (Abels *et al.*, 1941), as in the various nutritional diseases in alcohol addicts (Jolliffe, 1941).

Factors interfering with utilization are: hepatic dysfunction (a liver cirrhosis, chronic hepatitis, alcoholism); hypothyroidism; and malignant diseases of the gastro-intestinal tract.

Increased Body Requirements

In a strict sense adequate nutritional intake should cover increased body requirements. Under certain conditions, however, the metabolic requirements are increased far beyond the average limits, and these exceptions might be considered as conditioning factors. Fever increases the basal metabolism about 13% for each degree centigrade, strong emotion may also increase the metabolism considerably, while strenuous exercise or very hard work may even raise it to five to fifteen times above the basal level (Best and Taylor, 1943).

The influence of sunshine in the provocation of deficiency symptoms is well known. Its precipitating effect in pellagra ("mal di sole") is partly ascribed to its traumatic action (Smith and Ruffin, 1937) and partly to the excretion of the B vitamins in sweat (Cornbleet *et al.*, 1943).

A conditioned deficiency may be produced by thyroid, dinitrophenol, and fever therapy, which increases the whole metabolism, or by high carbohydrate diet, insulin-shock therapy, and parenteral administration of large amount of glucose, which increase the demand for coenzymes (Spies *et al.*, 1938). The water-soluble vitamin-B group, especially thiamin, may easily be washed out of the tissues and used up by repeated glucose infusions (e.g., after operations). The resulting "water-logging" (Sydenstricker, 1941) after excessive parenteral administration of glucose is a manifestation of thiamin deficiency.

Pregnancy and lactation have long been known to provoke symptoms of vitamin deficiency. Nixon *et al.* (1942), utilizing his material in Hong Kong and in this country, found besides pregnancy neuritis, already described in this country (Theobald, 1936), conditions allied to toxaemia and beriberi in undernourished pregnant women. It is not yet clear whether these symptoms are due only to increased requirements. Damage of the liver from pregnancy toxaemia may also lead to impaired liver function interfering with the utilization and storage of thiamin, choline, and other members of the vitamin-B group.

The importance of large doses of a single synthetized vitamin as a conditioning factor is still insufficiently recognized. Since Spies, Bean, and Ashe (1939) and Sydenstricker *et al.* (1940) first noticed that symptoms of thiamin and riboflavin deficiency became more pronounced in pellagrins after nicotinic acid treatment similar occurrences have been repeatedly recorded in clinical medicine. Lehmann and Nielsen (1939), Braendstrup (1940), and Salvesen (1940) described signs of pellagra after large parenteral doses of thiamin. Bichel and Meulengracht (1941) reported the development of pellagra after treatment with riboflavin; Leitner (1945) described signs of riboflavin deficiency after large parenteral doses of thiamin. Repeated attempts to produce imbalance of the vitamin-B factors experimentally have been unsuccessful, but Richards (1945) was able to induce fits in rats kept on pyridoxin-poor diet after large doses of thiamin, whilst the fits (characteristic of pyridoxin deficiency) could be entirely prevented if small doses of pyridoxin were given before the thiamin. Richards also suggested that one of the two types of thiamin toxicity described previously by Leitner (1943) which resembled thyroid overdosage might well be considered a vitamin deficiency induced by excess of the single vitamin.

Apart from the comparatively small number of verified descriptions of this syndrome, one encounters in hospital and private practice many partly abortive cases which often appear after repeated parenteral doses of one single vitamin—mainly thiamin.

A woman admitted to hospital with menopausal arthritis and gross adiposity was given a routine slimming diet, mersalyl, and thyroid. After having lost about 1 st. (6.35 kg.) in weight she still complained of shortness of breath; there were no signs of organic heart disease, and it was suggested that the shortness of breath was due to thiamin deficiency. Daily parenteral injections of 25 mg. of thiamin improved the breathlessness within five days, but painful cracks developed at the angles of the mouth, followed by crust formation and cheilosis.

Leitner (1946b, 1947a, 1947b) emphasized again that subclinical latent deficiencies within the vitamin-B group may often become manifest after energetic treatment of the obvious deficiency. Farrar (1947) found that administration of large doses of thiamin in inadequately nourished cases of pernicious anaemia aggravated the glossitis and caused diarrhoea and pellagrous dermatitis, but no pellagra-provoking effect of thiamin could be observed in the same patients when adequate diet had been given. He also found that haematological relapse appeared quicker when nicotinic acid was administered after stopping liver treatment. Davidson and Girdwood (1948) observed in two cases of pernicious anaemia and three cases of sprue the appearance, during treatment with folic acid, of

vitamin-B complex deficiency, consisting mainly of peripheral neuritis, cord involvement, angular stomatitis, cheilosis, and pellagrous dermatitis with depression. Whilst administration of purified vitamins was of little avail, potent liver extract always brought about an improvement. As the liver extract, containing only traces of the vitamin-B complex, produced the most dramatic effect on a wide variety of vitamin-deficiency symptoms, Davidson and Girdwood suggest that liver extract may contain a factor which liberates members of the vitamin B complex from their inactive form or facilitates their absorption or utilization. Leitner (1948b) subsequently put forward again the explanation that large doses of one purified vitamin (i.e., one single enzyme system) may easily upset the balance in deficiency states or may exert an inhibitory effect on other enzyme groups which at that particular time are present in abnormally low amount. The well-balanced multiple enzyme systems present in potent liver extracts may restore the disturbed equilibrium without containing large doses of any of the known purified vitamins.

TABLE III.—*Factors Increasing Body Requirements*

Increased activity:
Strenuous and prolonged physical efforts, psychosis, delirium.
Certain environmental influences:
Certain manufacturing processes and industries, excessive winds, light glare (snow).
Fever.
Pregnancy and lactation.
Hyperthyroidism.
Therapeutic measures:
Thyroid, alpha-dinitrophenol, parenteral dextrose, or excessive continuous fluid intake as in urinary infections, high carbohydrate diets, fever therapy, large doses of a single pure vitamin.

Increased Excretion

Increased excretion of vitamins may secondarily lead to malnutrition, but there are very few substantiated observations to this effect. Lactation, polyuria, or forced water-intake (Cowgill *et al.*, 1930) may cause increased excretion of vitamins (e.g., in urinary infections, sulphonamide treatment). The occasional observation of a mild gestational polyneuropathy with rapid development of symptoms and signs during the first few weeks of lactation might be an example of increased excretion. Excessive perspiration in the Tropics might condition a deficiency of the water-soluble B vitamins, as some of them appear in sweat in a considerable contrentration after heavy physical exercise (Cornbleet *et al.*, 1943).

The main factors that increase excretion of vitamins are : (1) polyuria (diabetes mellitus, after excessive intake like urinary infections, sulphonamide therapy) ; (2) lactation ; (3) excessive perspiration.

Increased Destruction

Induced vitamin deficiency in animals has long been known. Generalized erythematous scaly dermatitis with pruritus, arrest of growth, spastic gait, and abnormal posture could be produced by feeding raw egg-white in animals (Boas, 1927) and man (Sydenstricker *et al.*, 1942). The cause of this syndrome is a biotin deficiency. The glycoprotein (avidin) contained in the raw egg-white forms a complex in the gastro-intestinal tract with biotin, and this complex cannot be broken down. Cooked egg-white, on the other hand, does not inactivate biotin. Another severe deficiency is chastek paralysis in silver foxes fed on raw fish. It consists of anorexia, hyperaesthesia, ataxia, and death, with cerebral lesions similar to Wernicke's encephalopathy, and it is due to thiamin destruction caused by the thiaminase in raw fish (Melnick *et al.*, 1945). It is prevented by injection of vitamin B_1 (Evans *et al.*, 1942) or by cooking the fish. Although both conditions are very probably not due to simple destruction of the vitamin, it is perhaps pertinent to mention them here—"antivitamins," "inhibitors" (Woolley, 1944).

Factors leading to increased destruction of vitamins are : (1) achlorhydria ; (2) alkalis, sulphonamides ; (3) toxic doses with lead ? arsenicals ? gold ?

Achlorhydria seems to interfere with the assimilation of ascorbic acid. Alt *et al.* (1939) have shown 65% destruction of ascorbic acid in three hours at a *p*H of 7.95, and Melnick *et al.* (1941) found that thiamin is stable in acid gastric juice (*p*H 1.5 to 8) during an incubation of 16 hours, but if antacids were added thiamin was completely destroyed. Bile and pancreatic juice also destroyed a considerable part of thiamin.

It has been claimed that vitamins, especially vitamin C, are often destroyed owing to their "detoxifying" actions—e.g., by arsenicals, gold, lead, sulphonamides, barbiturates, T.N.T., etc.—but the evidence is conflicting (Bicknell and Prescott, 1946).

The discovery of biosynthesis of vitamins by the intestinal flora focused some attention on sulphonamide therapy. It was known for some time that sulphonamides reduced the therapeutic action of nicotinic acid. Whilst there could be competition for the same enzyme system (Wood, 1940) between sulphapyridine and nicotinic acid, the explanation did not hold good for sulphonamides not containing the pyridine ring. Later it could be shown in man that, after giving sulphaguanidine or sulphasuxidine, the vitamin biosynthesis—e.g., that of thiamin (Najjar and Holt, 1943), riboflavin (Najjar *et al.*, 1944). nicotinic acid (Ellinger *et al.*, 1944)—in the intestines was substantially reduced or perhaps completely inhibited. As the extent of the biosynthesis is at present unknown the loss of this function may be considered from a practical point of view equivalent to destruction.

Diagnosis

Diagnosis of early vitamin-deficiency states is exceedingly difficult. The deficiency should be diagnosed at a time when symptoms have not yet been developed into the textbook description of deficiency disease ; in the latter case the patient would be severely ill. The early symptoms are often non-specific, and laboratory methods are usually of little help at this stage, and to recognize the condition reliance has to be placed on the patient's dietary history, on indefinite symptoms and signs found on physical examination, and on a balanced clinical judgment. Complete nutritional failure is a rare condition in this country, but different degrees of deficiency state with a host of vague symptoms are frequent enough to warrant serious concern. In the earlier stages of vitamin research there was an inclination to attribute definite symptoms to a particular vitamin, but clinical experience has taught us that with greater frequency it takes the form of borderline states of ill-health owing to multiple deficiencies, often with vague symptoms which might easily be attributed to other causes.

Personal and Dietary History

The U.S. Public Health Service states that nutritional diseases constitute their greatest medical problem, not from a point of view of death but from that of disability and economic loss (Wohl, 1945). The fact that no similar statement has been made by public health authorities in this country does not by any means imply that the problem is non-existent here.

Grossly inadequate diet can be recognized without difficulty. Particular consideration should be given to patients on any special diet—e.g., those with obesity, peptic ulcer, dyspepsia, diabetes, etc. Detailed attention should be paid to dietary history in cases of psychoneurosis.

Clinical Examination

As manifold deficiency symptoms usually occur simultaneously, a wide variety of vague and interwoven symptoms are met with. The earliest symptoms consist of such general complaints as anorexia, fatigue, loss of weight, restlessness, irritability, paraesthesias, cramp in the muscles, burning of the eyes, photophobia, dimness of vision, impairment of memory, etc. These vague symptoms may be caused by different deficiencies, and they become pronounced with advancing disease.

In a *vitamin-A deficiency* clinical signs are detectable only when the process is moderately advanced. Perhaps the earliest change is xerosis conjunctivae, which can be observed if the eyelid of the patient is kept open for a few minutes ; the lustre is lost owing to the rapid drying of the conjunctiva. This is due to metaplasia and thickening of the conjunctival epithelium, which reduces the secretion. It may be the earliest sign of vitamin-A deficiency. Like night-blindness—another symptom of vitamin-A deficiency—it is not specific, and both might have several other aetiological causes. Xerosis conjunctivae may later develop into Bitot's spots, which may or may not be

associated with night-blindness. Burning of the eyes, lacrimation, photophobia, and discharge are further early eye symptoms. More advanced changes of vitamin-A deficiency are to be seen in the skin, which becomes dry, scaly, and horny, with sharp oval-shaped papules around the follicles. Late stages of vitamin-A deficiency are connected with more pronounced damage of epithelial structures, mainly of the mucous membranes.

In a survey of 195 hospital and private patients with complaints not expected to interfere with the vitamin-A level, normal blood carotene and vitamin-A values were found (Leitner and Moore, 1948a). No signs of vitamin-A deficiency could be detected in any of these cases clinically. We found, however, low vitamin-A values in certain rare skin diseases (Leitner and Moore, 1946, 1948b) with characteristic skin lesions (Leitner, 1947c).

The early changes of *vitamin-B deficiency* are the most frequently met with in practice. It has been mentioned that the various members of the vitamin-B complex are grouped together more by virtue of their association in nature than by any structural similarity. Owing to their close association deficiency symptoms of the various members of the group overlap even more than would at first be expected.

The earliest signs of thiamin deficiency are generally ill-defined, and they are due most probably to deficiency of the entire B complex. The prodromal period may be described as a period of ill-health lasting for a long time. As thiamin is mainly concerned with metabolism of the nervous tissue, early deficiency symptoms chiefly connected with the abnormal function of the nervous tissues, such as anorexia, fatigue, irritability, dizziness, apprehension, etc., might be expected to form part of the clinical picture. But these symptoms are absolutely unspecific, like many of the early symptoms of other vitamin deficiencies, and the laboratory methods available are not sensitive enough to determine their origin. It may be argued that ill-health is the earliest symptom of many of the slowly developing pathological conditions, the specific symptoms and signs developing much later. It has, indeed, been my experience that more definite symptoms and signs follow if the symptoms mentioned remain untreated, and therapeutic tests corroborate this assumption. Though these early symptoms attributed to deficiencies are often encountered, properly controlled large-scale surveys have never been carried out.

Anorexia, fatigue, loss of weight, inability to concentrate, nervousness, transient digestive disturbances, intermittent pain and burning sensation, soreness at the corners of the mouth, burning pains in the eyes with visual disturbances, headache, dizziness, insomnia, and depression are early signs attributed to riboflavin deficiency. Sebrell and Butler (1938) differentiated by feeding experiments the well-known symptoms which later were termed hyporiboflavinosis (Stannus, 1944): paleness of the lips and angles, followed by maceration and bilateral superficial fissures. The macerated lesion becomes subsequently dry, a crust forms at the angles (angular stomatitis); the lips remain pale, red, denuded, cracked, and crusted with transverse markings (cheilosis). The tongue is clean, the papillae are flattened, with patchy denudation and congestion of the capillary loops leading to magenta colour in contrast to the shiny, atrophic, often painful scarlet-red tongue in pellagra. A fine scaly, somewhat "branny" desquamation on an erythematous base on the alae nasi, on the naso-labial folds, eyelids, ears, occasionally the hands, vulva, and perineum, are other early signs (Sebrell and Butler, 1938). Ocular disturbances (Spies, Vilter, and Ashe, 1939) such as conjunctivitis, burning, photophobia, pruritus, sensation of sand, and corneal vascularization leading later to punctate opacities are regarded by some authorities as the earliest signs of hyporiboflavinosis (Sydenstricker *et al.*, 1940).

Nicotinic acid deficiency is also introduced by a long period of "deficiency development time" characterized by loss of appetite and weight, disturbances of the alimentary tract, general muscular weakness, lassitude, irritability, insomnia, depression, inability to concentrate, vertigo, numbness, palpitation, flight of ideas, anxieties, loss of memory, and confusion. At this stage no physical signs are present and the diagnosis of malingering, neurasthenia, or anxiety neurosis is easily made. The characteristic mucous membrane and dermal lesions appear much later. Hyperaesthesia of the tongue may precede the swelling, redness, and indentation caused by the teeth. Desquamation of the superficial layer causes a scarlet-red, dry, smooth, beefy tongue which is often painful. Secondary infection with monilia and Vincent's organisms over the fissures and aphthous ulcers occurs frequently, and the inflammatory process often extends to the neighbouring mucous membranes. The associated angular stomatitis and cheilosis might respond to riboflavin treatment. (Angular stomatitis may also be caused by ill-fitting dentures, dribbling, chewing-gum, and lipstick.) The characteristic skin lesions may sometimes be missed (pellagra sine pellagra). They are more often than not symmetrical, and may be precipitated by sunlight or other irritation. Hands, face, neck, knees, feet, and perineal regions are favourite places, but the sunburn-like, erythematous, pigmented, often hyperkeratotic, and distinctly demarcated lesions may appear anywhere. Mental symptoms such as emotional instability, depression, and confusion may be precipitated suddenly (Gottlieb, 1944), or within a few days in persons on deficient diet.

A woman, aged 64, who lived for 10 years on a restricted diet developed pulmonary tuberculosis. She was admitted to a sanatorium and improved greatly on a full diet. After eight months' sanatorium treatment she suddenly developed diarrhoea accompanied by anorexia. Within a few days changes occurred in the oral mucous membrane, followed by depression and confusion, and the skin and eye changes characteristic of pellagra were fully developed (Rimington and Leitner, 1945).

It would exceed the scope of this paper to discuss the possible relationship of macrocytic and microcytic anaemias to vitamin and nutritional deficiencies. It is perhaps sufficient to refer to the results achieved with another B vitamin—folic acid—in macrocytic anaemia, in the sprue syndrome, and in allied conditions.

Early *vitamin-C deficiency* is another widespread condition. Owing to the scarcity of citrus and other fruit and fresh vegetables for many years, congested, swollen, purple-red, easily bleeding gums occur comparatively often. I have also seen florid scurvy on five occasions during recent years, mainly in old single men who normally cooked only once a week for themselves and lived predominantly on warmed-up, overcooked meals. Fatigue, weakness, and anaemia are often early unspecific signs of vitamin-C deficiency, together with localized follicular keratosis. Petechial haemorrhages are usually moderately advanced signs, and although increased capillary fragility is more and more attributed to vitamin-P deficiency (Scarborough, 1940), the two substances appear to be associated in nature.

Laboratory Tests

These are of little help in early vitamin-deficiency states. Urinanalysis is usually normal. The blood picture may or may not show a moderate microcytic or normocytic anaemia. Blood sedimentation rate, total serum proteins, and albumin globulin ratio are usually within normal limits. The fractional test meal often shows an achlorhydria, but this is neither pathognomonic nor characteristic. It is said that oesophagoscopy and gastroscopy usually reveal the same changes as are found in the buccal cavity. The "deficiency pattern" of the small intestine found on *x*-ray examination with abnormal segmentation, pooling, disappearance of herringbone structure, obliteration and coarsening of the mucosal folds (Golden, 1941), although not always characteristic, may offer some indication of a B-complex deficiency.

During the last few years exact laboratory tests have been worked out for the determination of a given vitamin in the blood; saturation and excretion tests were also introduced. The assessment of the vitamin status, especially in the case of early deficiency, is, however, not simple. While the results of saturation tests as shown recently by Ellinger and Hardwick (1947) for nicotinamide may be affected by unknown mechanisms, low vitamin values in the blood and urine may, on the other hand, be found without depletion of stores in the organs; these findings are at times singularly uncharacteristic in cases of early deficiencies, and can be used only with great caution in the assessment of physiological deficiency. Moreover, it is essential that the laboratory data should be carefully correlated with the clinical findings. Within these limits, however, it is obvious that exact laboratory tests can

substantially contribute to the detection of subclinical deficiency states. For vitamin A the chemical estimation of the vitamin in plasma and the estimation of the dark-adaptation, for thiamin and riboflavin the determination of the excretion of vitamin B_1 and B_2, are the routine laboratory tests. Saturation tests are used for the assessment of nicotinic acid and ascorbic acid; some also rely on the vitamin-C estimation in the white cell layer, on the determination of capillary fragility, and on *x*-ray changes in the bones. The great difficulty with these procedures is that they nearly always require specialized laboratory technique.

Differential Diagnosis of Early Symptoms

As naturally occurring deficiency is always multiple, the associated symptoms are, especially in the early stages, often interwoven, and this makes the diagnosis of a deficiency of a specific chemical substance most difficult. Vague, ill-defined, waxing and waning complaints, prominent among them being fatigue, weakness, loss of appetite, loss of initiative, irritability, personality changes—in fact, all the common symptoms of neurasthenia—are frequently encountered. The patients are neurasthenics, indeed, and it is often difficult to separate these two conditions, particularly as neurasthenics are liable to eat an inadequate diet. Weir Mitchell long ago established that some neurasthenics benefited by a properly balanced forced diet combined with rest; and after careful study of the modern version of Weir Mitchell's method—the modified insulin treatment in neurotics (Sargant and Slater, 1944)—one wonders whether seclusion and reassurance or proper food are more important for their cure.

TABLE IV.—*Symptoms described as Manifestations of Early Vitamin Deficiency (after Cayer, 1946)*

Fatigue*	Paraesthesia*	Depression*	Weakness*
Insomnia*	Palpitation*	Abdominal discomfort	Lassitude*
Anorexia*	Nervousness*	Muscular weakness*	Muscle pain
Vertigo*	Irritability*	Backache	Lack of concentration*
Headache	Dyspepsia*	Apprehension*	Anxiety
			Confusion
			Decreased output of work

*Symptoms given as symptoms of neurasthenia in the textbooks of medicine.

Table IV may facilitate the appreciation of the overlapping between symptoms of early vitamin-deficiency states and neurasthenia (Cayer, 1946). This overlapping unfortunately led to the indiscriminate use of vitamin preparations all over the world. All evidence, however, shows that administration of vitamins without underlying* deficiencies does nothing to improve the patient.

The difficulty in the assessment of early deficiency states warrants the occasional administration of vitamins as a therapeutic test. If the quick disappearance of symptoms is followed by general well-being the suspected diagnosis might have been right. Great care, however, has to be exercised, as slight improvement often follows any therapeutic trial.

Treatment

The underlying principle of the treatment of early vitamin-deficiency states is to deal with the conditioning factors and to supplement the tissue deficiencies. The degree of depletion of the various food factors varies in different patients, and, whilst often only one deficiency symptom predominates in the clinical picture, it has to be borne in mind that other deficiencies are also likely to be present. Food contains many still unknown factors certainly necessary for proper nutrition, and these are not present in synthetized vitamin preparations. The basis of treatment consists accordingly in securing an adequate diet.

It is quite evident that provision of the average daily requirements is not sufficient to make up for past losses. Although some of the patients showing early vitamin deficiencies may appear obese and overnourished, an investigation of their food intake will show that they have an imbalanced diet. The intake in these cases ought to be at least 3,500 calories, containing 120–130 g. of proteins (calculated for a person of 11 st.—70 kg.). This diet cannot be given easily to patients in this country at present; our rations, even with additional foods for invalids, cannot provide either the necessary calories or the suggested protein intake. It is to be hoped, however, that the world food situation will soon enable the food policy of this country to be altered, at least for those who are in special need. Table V indicates the foods rich in different vitamins.

TABLE V.—*Food Rich in Vitamins*

Vitamin A	Thiamin	Riboflavin	Nicotinic Acid	Ascorbic Acid
Butter	Wholemeal	Wholemeal	Bran	Blackcurrant
Milk	Oatmeal	Bran	Peanuts	Rose-hip
Cheese	Bran	Nuts	Chicken	Lemon
Eggs	Peas	Beans	Pork	Orange
Carrots	Beans	Peas	Beef	Lime
Broccoli	Lentils	Broccoli	Liver	Grapefruit
Lettuce	Parsnip	Endive	Kidney	Strawberries
Spinach	Nuts	Spinach	Heart	Tomatoes
Tomatoes	Milk	Mushrooms	Meat extracts	Green pepper
Liver	Eggs	Milk	Salmon	Red pepper (paprika)
Eel	Fish-roe	Cheese	Mackerel	Potatoes
Carp	Pork	Eggs	Brewer's yeast	Cabbage
Fish-liver oils	Veal	Fish-roe		Sprouts
	Beef	Kidney		Cauliflower
	Brewer's yeast	Liver		Turnips
		Meat extracts		Parsley
		Brewer's yeast		Spinach
				Dandelion

In addition to a rich and well-balanced diet, vitamins should be administered in deficiency states. Parenteral administration of vitamins should be restricted to emergencies and to those cases in which there is obvious interference with absorption. As indicated earlier, large doses of parenterally given pure vitamins, especially those of the B group, may provoke a serious imbalance, and even if there is a deficiency of the administered vitamin they sometimes cause more harm than good. This point should be specially stressed, as there are indications that latent deficiencies without obvious clinical signs and symptoms are much more widespread than is realized. In early vitamin deficiencies something like five to ten times the daily minimal requirement should be given—e.g., thiamin and riboflavin 10–15 mg., nicotinamide 100–200 mg., ascorbic acid 150–300 mg., in divided doses three times a day. Fat-soluble vitamins should be given in larger doses, and my practice is to give 50,000 to 100,000 i.u. of vitamin A daily. As vitamin-A deficiency is often connected with disturbance of liver function, simultaneous parenteral application of liver extract seems, in my experience, to reduce the time needed for correction of the deficiency (Hoagland, 1945). Vitamins D and K are outside the scope of this paper, and no therapeutic suggestion is therefore given for deficiency of these.

In cases of deficiency of one of the vitamins of the B group it is advisable to give, instead of the most obviously lacking factor, a mixture of thiamin, riboflavin, nicotinamide, and possibly folic acid, together with brewer's yeast, 1–1½ oz. (28–42 g.), or liquid liver extract, 1 oz. (28 ml.), daily. Injection of the less refined liver extracts may also be tried. Symptoms usually begin to improve after two to four weeks, but as the depletion may be of long standing it is advisable to continue giving smaller doses for a longer period, particularly as dietary treatment alone in this country is bound to be ineffective for some time to come.

Summary

Deficiency states may be caused solely by the failure to ingest an adequate diet, or may be conditioned by factors which interfere with ingestion, absorption, and utilization, or by conditions which increase the requirements for vitamins and their excretion or destruction. The physiological and pathological aspects, and the therapeutic measures that may result in a conditioned deficiency state, are briefly discussed.

The clinical diagnosis of early deficiency states is exceedingly difficult, as the deficiencies tend to be multiple and the symptoms in many instances are non-specific. Physical signs are often

absent, and laboratory findings may not be characteristic in the early stages. Diagnosis should not be made on the basis of symptoms alone; careful evaluation of the dietary history, symptoms and signs, the available laboratory data, and response to specific therapy may help to establish the cause.

Not only a number of diseases but also some of the therapeutic measures used to combat them may precipitate a deficiency state, and the imbalance of vitamin-B factors is particularly stressed. The treatment of early vitamin-deficiency states is in every case an individual medical problem requiring exact diagnosis and properly planned therapeutic measures.

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REFERENCES

Abels, J. C., Gorham, A. T., Pack, G. T., and Rhoads, C. P. (1941). *J. clin. Invest.*, **20**, 749.
Alt, H. L., Chinn, H., and Farmer, C. J. (1939). *Amer. J. med. Sci.*, **197**, 229.
Andersen, O. (1939). *Acta paediatr., Stockh.*, **24**, 422.
Beams, A. J., Free, A. H., and Glenn, P. M. (1941). *Amer. J. digest. Dis.*, **8**, 415.
Bennett, T. I., and Hardwick, C. (1940). *Lancet*, **2**, 381.
Best, C. H., and Taylor, N. B. (1943). *The Physiological Basis of Medical Practice*, pp. 902, 1063. London.
Bichel, J., and Meulengracht, E. (1941). *Klin. Wschr.*, **20**, 913.
Bicknell, F., and Prescott, F. (1946). *The Vitamins in Medicine*, pp. 482, 210. Heinemann, London.
Boas, M. A. (1927). *Biochem. J.*, **21**, 712.
Braendstrup, P. (1940). *Ugeskr. Læg.*, **102**, 95.
Breese, B. B., jun., and McCoord, A. B. (1939). *J. pediat.*, **15**, 183.
Cayer, D. (1946). *J. Amer. med. Ass.*, **132**, 558.
Cornbleet, T., Kirch, E. R., and Bergeim, O. (1943). Ibid., **122**, 426.
Cowgill, G. R., Rosenberg, H. A., and Rogoff, J. (1930). *Amer. J. Physiol.*, **95**, 537.
Davidson, L. S. P., and Girdwood, R. H. (1948). *Lancet*, **1**, 360.
DuBois, E. F., and Chambers, W. H. (1942). *J. Amer. med. Ass.*, **119**, 1183.
Ellinger, P., Coulson, R. A., and Benesch, R. (1944). *Nature, Lond.*, **154**, 270.
—— and Hardwick, S. W. (1947). *British Medical Journal*, **1**, 672.
Elliott, M. C., Isaacs, B., and Ivy, A. C. (1940). *Proc. Soc. exp. Biol., N.Y.*, **43**, 240.
Evans, C. A., Carlson, W. E., and Green, R. G. (1942). *Amer. J. Path.*, **18**, 79.
Farrar, G. E., jun. (1947). *Penn. med. J.*, **50**, 1053.
Glover, J., Goodwin, T. W., and Morton, R. A. (1947). *Biochem. J. Proc.*, xlv.
Golden, Ross (1941). *Radiology*, **36**, 262.
Gottlieb, B. (1944). *British Medical Journal*, **1**, 392.
Haig, C., and Patek, A. J. (1942). *J. clin. Invest.*, **21**, 309.
Hoagland, C. L. (1945). *Bull. N.Y. Acad. Med.*, **21**, 537.
Jolliffe, N. (1941). *Quart. J. Stud. Alcohol*, **1**, 517.
—— (1942). In New York Academy of Medicine, *Preventive Medicine in Modern Practice*, p. 79. Hoeber, New York.
Laurent, L. P. E., and Sinclair, H. M. (1938). *Lancet*, **1**, 1045.
Lehmann, J., and Nielsen, H. E. (1939). *Nord. Med.*, **1**, 289.
Leitner, Z. A. (1942). *Trop. Dis. Bull.*, **39**, 497.
—— (1943). *Lancet*, **2**, 474.
—— (1945). *British Medical Journal*, **1**, 609.
—— (1946a). *Brit. J. Derm.*, **58**, 11.
—— (1946b). *Lancet*, **2**, 960.
—— (1947a). Ibid., **1**, 345.
—— (1947b). *British Medical Journal*, **1**, 945.
—— (1947c). *Brit. J. Derm.*, **59**, 407.
—— (1948a). *Med. Pr.*, **219**, 215.
—— (1948b). *Lancet*, **1**, 462.
—— and Moore, T. (1946). Ibid., **2**, 262.
—— —— (1948a). Spec. Rep. Ser. med. Res. Coun., Lond., No. 264. In press.
—— —— (1948b). *Brit. J. Derm.*, **60**, 41.
Manson-Bahr, P., and Clarke, O. (1946). *Lancet*, **2**, 903.
Melnick, D., Hochberg, M., and Oser, B. L. (1945). *J. Nutrit.*, **30**, 83.
—— Robinson, W. D., and Field, H. (1941). *J. biol. Chem.*, **138**, 49.
Moore, T. (1931). *Biochem. J.*, **25**, 275.
Najjar, V. A., and Holt, L. E. (1943). *J. Amer. med. Ass.*, **123**, 683.
—— Johns, G. A., Mediary, G. C., Fleischmann, G., and Holt, L. E. (1944). Ibid., **126**, 357.
Nixon, W. C. W., Wright, M. D., and Fieller, E. C. (1942). *British Medical Journal*, **1**, 605.
Richards, M. B. (1945). Ibid., **1**, 433.
Rimington, C., and Leitner, Z. A. (1945). *Lancet*, **2**, 494.
Salvesen, O. (1940). *Nord. Med.*, **5**, 279.
Sargant, W., and Slater, E. (1944). *Physical Methods of Treatment in Psychiatry*, p. 41. London.
Scarborough, H. (1940). *Lancet*, **2**, 644.
Sebrell, W. H., and Butler, R. E. (1938). *Publ. Hlth Rep., Wash.*, **53**, 2282.
Smith, D. T., and Ruffin, J. M. (1937). *Arch. intern. Med.*, **59**, 631.
Snell, A. M. (1939). *J. Amer. med. Ass.*, **112**, 1457.
Spies, T. D., Bean, W. B., and Ashe, W. F. (1939). *Ann. intern. Med.*, **12**, 1830.
—— Cooper, C., and Blankenhorn, M. A. (1938). *J. Amer. med. Ass.*, **110**, 622.
Spies, T. D., Milanes, F., Menendez, A., Koch, M. B., and Minnich, V. (1946). *J. Lab. clin. Med.*, **31**, 227.
—— Vilter, R. W., and Ashe, W. F. (1939). *J. Amer. med. Ass.*, **113**, 931.
Stannus, H. S. (1944). *British Medical Journal*, **2**, 103.
Stewart, J. D., and Rourke, G. M. (1941). *J. clin. Invest.*, **20**, 453.
Sydenstricker, V. P. (1941). *Ann. intern. Med.*, **14**, 1499.
—— Sebrell, W. H., Cleckley, H. M., and Kruse, H. D. (1940). *J. Amer. med. Ass.*, **114**, 2437.
—— Singal, S. A., Briggs, A. P., de Vaughn, N. M., and Isbell, H. (1942). Ibid., **118**, 1199.
Theobald, G. W. (1936). *Lancet*, **1**, 834.
Wohl, M. G. (1945). *Dietotherapy*, p. 421. London.
—— and Feldman, J. B. (1939). *Endocrinology*, **24**, 389.
Wood, D. D. (1940). *Brit. J. exp. Path.*, **21**, 74.
Woolley, D. W. (1944). *Science*, **100**, 579.

THE TREATMENT OF NEUROSYPHILIS WITH PENICILLIN*

BY

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The powers of penicillin have excited the whole world, but penicillin was introduced as an antibacterial remedy and it was not to be expected that it would be potent against the protozoal infection of syphilis. Moreover, it was soon discovered that penicillin given intramuscularly did not find its way into the cerebrospinal fluid; it did not, it was said, pass the blood–brain barrier; and so it was inherently improbable that it would have much effect on syphilis of the nervous system. We knew also that nowhere did the spirochaete entrench itself more strongly than in the brain; we knew that general paralysis especially was a hard nut to crack. It was therefore right and natural that the first rumours that penicillin was in some degree effective in cases of neurosyphilis, and even in cases of general paralysis, should be received with a certain amount of incredulity; and this attitude is apparent in most of the reports on the trials of penicillin in neurosyphilis, because nearly all observers, finding some clinical improvement but little immediate change in the cerebrospinal fluid and blood, have gone on to treat their patients with malaria. General paralysis is a progressive and inexorable disease that allows no temporizing, and one must have good reason for withholding the well-tried standard, if desperate and often inadequate, remedy.

My own attitude at the beginning was the same. Early in 1945 some penicillin became available for civilian hospital use in diseases for which it was known to be appropriate, and just at that time I had admitted to the National Hospital under my care a man of 50 suffering from taboparesis.

This patient was euphoric and fatuous, and had recently lost his position as a secretary-accountant because of his inability to carry out his duties. He was pursuing allotment gardening in a hypomanic way, and had undertaken several allotments though he was a small weak man. At home he was restless, irritable, obstinate, and sometimes tearful. He had some tremor of his lips and tongue and a tremulous dysarthria, and also some tremor of his hands. His pupils were inactive to light, his knee-jerks and ankle-jerks were absent, and his plantar reflexes were weakly extensor. His cerebrospinal fluid showed typical paretic characteristics and his blood Wassermann reaction was strongly positive. I decided to try the effect of penicillin, and we were able to obtain the required amount. The reports which had come from America had at first suggested that over a million units might be necessary, but by the time treatment was started on this patient it was being said that even two million units were required, and he was given a course

*A paper read to the Society for the Study of Venereal Diseases on Jan. 24 (abbreviated).

of two million units in injections of 20,000 units every three hours. When the course was finished he had certainly made some clinical improvement. He was less restless, a little less expansive, and his concentration and memory were better. Physically he was less tremulous, but the other physical signs were of course unchanged. To our disappointment his cerebrospinal fluid, examined ten days after the completion of his course of penicillin, showed practically no change.

The Americans had had a long start of us, and the few reports which were then available indicated that penicillin was inadequate, and that it was necessary to use malaria as well. Faced with the lack of serological improvement in my patient and with this information from America, I thought it obviously the appropriate course to proceed with malarial therapy, and this was done without waste of time. I did nevertheless say, being impressed with the clinical improvement, that it would be a pity to cure the patient with penicillin and then, for the sake of confirming the cure, to kill him with malaria. As it turned out, this very nearly happened. At the time of his fifth rigor the patient passed into a semicomatose state with low muttering delirium, and the malaria was hurriedly arrested. Nevertheless he remained in a condition first of semicoma and muttering, and later, for nearly a fortnight, in a condition of profound dementia with lapses into delirium, and it seemed as if he was unlikely to survive. However, he gradually came round, and in the end made a very good recovery, although I do not think his mental state has ever been quite so good as it was before the malaria started.

This was by no means my first *contretemps* with malaria, but it was a new lesson. Meanwhile Dr. Carmichael had started one of his patients on penicillin—a case of frank G.P.I. in a man of 58—and invited me to follow the case with him. This man, when a course of three million units was finished, also showed clinical improvement, but his cerebrospinal fluid still had "paretic" abnormalities, and his blood Wassermann reaction was still strongly positive. Nevertheless we decided that we should treat the patient and not the cerebrospinal fluid, and clinically we saw no call for immediate further treatment, and certainly no justification for submitting him to the dangers from which the first patient had so narrowly escaped. After a short period of observation in the hospital, during which he continued to improve, he was allowed to go home. His improvement continued and after a few months he was very much better clinically. Since then I have treated well over 30 cases and none of them has had malaria, so that the following series of cases were treated either with penicillin alone or with penicillin supplemented only by the usual chemicals.

Present Series

The series consists of 24 cases which I had treated at the National Hospital, Queen Square, before the end of September last. The number is small compared with some of the American series, but this will not surprise those who are aware of the extent of the decline of neurosyphilis in this country (an interesting subject in itself which I hope to discuss at another time). Even in the American reports the number of cases described as treated by penicillin alone is not so very large, most of the big series consisting of cases treated by combined methods.

The cases hitherto published in England are few. Smith (1947) reported seven cases of general paralysis treated by penicillin alone and observed for periods up to 13 months. Lescher and Richards (1947) described 10 cases of neurosyphilis of different types treated with penicillin alone and other cases treated by combined methods. Nicol and Whelan (1947) have referred to the immediate effects in 14 cases treated with penicillin alone, and a larger number with a combined method.

My series is a mixed bag of all varieties of neurosyphilis. There were eight patients who presented mental symptoms, and they all had "paretic" spinal fluids; one other patient whose presenting symptom was hemiparesis, due evidently to a vascular lesion, also had a "paretic" fluid. Five patients were typical cases of tabes and two others were predominantly cases of optic atrophy, while nine patients were instances of different varieties of meningo-vascular syphilis.

Group 1, Dementia Paralytica.—Under this heading I include all cases with dementia and "paretic" changes in the cerebrospinal fluid. The group consists of eight cases—Nos. 1, 3, 7, 9, 14, 18, 20, 21, in chronological order—all of which have been followed up for at least six months and five of them for more than 12 months. The patient in Case 1 works two allotments himself and acts as secretary for the local allotment holders; in Case 3 the patient has for a long time past been back at his former work as a timekeeper. Case 7 was one of paresis in a woman of 60, who has shown great clinical improvement in the 20 months that have elapsed since her first treatment; whereas before her treatment she had to be cared for at home, she is now able to do her own housework and her shopping. Case 9 was one of paresis in a woman of 42; Case 14 was one of congenital infection in a woman of 27; in Case 20 the patient was a man of 59 who had received fever treatment by means of "sulfosin" in 1933; in Case 21 the dominant clinical features were tabetic and the mental symptoms were slight. In all these cases the patients concerned have made clinical improvement and all are working. The changes in the cerebrospinal fluids and bloods are shown in the Table. It will be observed that all the fluids have

Table Showing Changes in "Paretic" Cerebrospinal Fluids

Case No.		Cells	Protein mg.	Globulin		W.R.	Lange	Blood	
				N.A.	Pandy			W.R.	Kahn
1	Before .. 2M	13	60	+	+	4444	4555554321	4444	
	After—								
	1–2 weeks 5 rigors	4	50	±	+	4420	1223322221	4442	
	2 months	0	60	+	+	4444	1223443321	4444	
	5 ,,	0	70	+	+	4442	4555554210	4442	
	24 ,,	3	45	+	+	Neg.	5554432110		
	30 ,,	0	55	–	±	Neg.	5554321000	Neg.	
3	Before .. 3M	3	70	+	+	4420	3333432211	4431	
	After—								
	1–2 weeks 9 months	1	60	±	+	3200	5555554310	4420 Neg.	+
	12 ,,		Not known					3100	+
	22 ,,							Neg.	
7	Before .. 3M	12	90	+	+	++++	55200000		
	After—								
	1–2 weeks	15	120			++++	43320000		
	2 months 4M	4	100			++++	43210000		
	5 months 5M	0	70	–	±	4200	No change	4442	
	6½ months	3	65	–	±	Neg.	,, ,,	4443	+
	10 ,,	3	40	–	–	Neg.	,, ,,	4444	+
	14 ,,							4420	+
	20 ,,	0	50	–	–	Neg.	0001100000	3100	
9	Before .. 4M	38	80	+	–	4444	4544322100	4444	
	After—								
	1–2 weeks	16	80	+	+	4322	3443210000	3321	
	7 months 4M	3	60	+	+	4200	4433211000	4200	
	8 months	3	55	+	+	Neg.	4554321100	2000	+
	12 ,,	6	40	–	±	Neg.	2233321100	4200	±
	15 ,,							3100	+
14	Before .. 4·6M	14	30	–	–	4200	5555432100	4444	
	After—								
	1–2 weeks	3	25	±	±	4420	2321100000		
	12 months	3	25	–	–	Neg.	3433210000	4310	+
17	Before .. 4·6M	24	40	+	+	4442	4555432110	4444	
	After—								
	4 months	4	30	–	–	Neg.	4432100000	4442	
	9 ,,	1	25	–	±	2000	1223221000	4420	
20	Before .. 5M	6	40	–	±	4420	5554432100	Neg.	Neg.
	After—								
	3 months	2	40	–	±	4442	4543210000	Neg.	Neg.
	9 ,,	0	35	–	–	Neg.	No change		
21	Before .. 5M	296	85	–	+	4200	5555432100	4200	
	After—								
	6 months	5	45	±	±	Neg.	1122110000		
	7 ,,							Neg.	

become normal except for the persistence of Lange (colloidal gold) curves in some cases and the presence of six cells at the last examination in Case 9.

Group 2, Tabes.—Of the five cases in this group—Nos. 6, 8, 10, 15, 19—three had received previous treatment. No. 19 has been lost sight of. None of the patients concerned had a very active syphilitic cerebrospinal fluid, and their fluids and bloods have become normal with relative ease. Tabes being a slow degenerative disease, not much positive clinical improvement can be expected, but the patients are better subjectively and their lightning pains are diminished. From the nature of the disease it will take many years to determine whether or not it is arrested.

Group 3, Optic Atrophy.—Two patients—Nos. 5 and 11—presented with optic atrophy. The greatest interest attaches to the first of these, a man who when first seen was blind in his right eye and complaining of diminishing vision in the left. Both disks were paper-white, and there seemed little chance of saving any sight. With particular precautions at the start and preliminary iodide and mercury, he was given five million units of penicillin, and excision of the stellate sympathetic ganglion was performed on the left side with the purpose of increasing the blood supply to the left optic nerve. No further diminution of sight was observed, and in the course of some months his acuity of vision in the left eye, which was at first 6/12, recovered to 6/9 and later to 6/6, and at present it is a little better than 6/6. The visual field has remained full. In the other eye, too, there was a little recovery of sight, which enables him to see hand movements in a part of the field. I have seen improvement of vision before in cases of optic atrophy followed subsequently by deterioration, and therefore cannot be quite confident about the outlook in this case; but it is now 2¼ years since the first treatment, so that one can be hopeful. Nevertheless it is evident that in this case penicillin had an effective and prompt action. Case 11 is also noteworthy because it is the only one in the series in which symptoms continued to progress after a course of penicillin. The patient came under observation again after eight months and was given a second course of penicillin and also mercurial inunction, and in the succeeding eight months there has been no further deterioration of his sight.

Group 4, Meningo-vascular Syphilis.—Of the nine cases of meningo-vascular syphilis, three—Nos. 4, 16, and 17—presented vascular symptoms. Case 16 had generalized vascular disease with a high blood pressure, a type of case in which probably little improvement can be expected. Case 17 had paretic changes in her cerebrospinal fluid which are shown in the Table. Clinically and serologically she has improved greatly. Of the remaining patients in this group the first two were cases of subacute spinal syphilis, and these have shown only moderate improvement. A young man with an unusual visual disturbance has also improved moderately. The other three were all women with cerebral syphilis, two of whom had papilloedema, and all three of these patients have improved greatly after treatment.

Results in General

Reviewing these 24 cases, we may consider the apparent effects of the treatment in more general terms—the clinical effects, the effects on the cerebrospinal fluid, and the effects on the blood.

Clinical Effects.—In most cases it is evident that the progress of the symptoms has been arrested; we may exclude from consideration in this respect the cases of tabes and the cases which have been lost sight of, and we are then left with 18 cases in which clinical progress can be assessed. In Case 11 visual impairment continued to progress after the first treatment with penicillin was given, but in all the other cases the progress of symptoms has been arrested from the time of the first course of treatment, and in nearly all of them the patient has made positive recovery. Arrest of symptoms is all that can be expected clinically in the first instance from the most effective treatment, and it is the criterion of the effectiveness of treatment. Any positive recovery that occurs afterwards depends on the state of the nervous tissue after the disease process has been stopped, and its degree is not a measure of the effectiveness of the treatment. Whether the arrest of the clinical progress of the disease will be permanent it is impossible yet to say, but as yet there have been no relapses and no deaths so far as I know.

Effects on the Cerebrospinal Fluid.—The effects on the C.S.F. and blood form the best criterion of the probable permanence of the arrest of the disease and of its eradication. In most instances the Wassermann reaction in the cerebrospinal fluid has become negative in about a year. It is not known when it became negative in Case 1, but it was found negative at the end of two years. The number of cells in the fluid usually becomes normal quickly and has always been within normal limits by the end of two months. The total protein content becomes normal more slowly, and frequently shows an increase immediately after treatment, which may last for one or two months. This is probably to be regarded as an indication of the reaction that has gone on in the tissues, and particularly in the cerebrum, and it is in keeping with what occurs in various other diseases. The tests for excess globulin usually become normal about the same time as the total protein. The colloidal gold reaction shows the most persistent of the changes in the cerebrospinal fluid, and in Cases 1 and 14 it is still of the paretic type after 30 and 12 months respectively, when all other features of the fluid are approximately normal. As is well known, this also happens after malarial treatment, and the significance of this persistence is difficult to determine. In most instances, if the fluid is otherwise inactive, the reaction dies out in the course of some years, and it seems unlikely that an active colloidal gold reaction is to be regarded as any sign of activity of the disease. With the exception of the colloidal gold reactions, and occasionally of the total protein, all the cerebrospinal fluids in my series have returned to a normal state within about 12 months. The sequence of changes in the cerebrospinal fluid after penicillin therapy is thus exactly the same as that which follows successful treatment with malaria, and we may recall Dattner's insistence that a fluid which has become negative after malaria never becomes positive again.

Effects on the Blood.—It seemed at first that penicillin did not have much influence on the Wassermann reaction of the blood, but as time has gone on the reaction in the blood has become negative in a number of patients who have had no treatment except penicillin, and in some other patients it now shows a decided weakening. In cases in which N.A.B. and bismuth were given in addition the state of the blood is no better than in the others. In general the blood reactions in the series as a whole seem now as good as would have been obtained by any other method of treatment, but the delay in the correction of the blood Wassermann reaction after that of the cerebrospinal fluid has become normal is difficult to understand. A similar delay is known to occur after malarial treatment, but after penicillin it is more striking, possibly because other changes occur more quickly than after malaria.

The combined effects of the treatment on the clinical state and on the states of the cerebrospinal fluid and blood all indicate that treatment with penicillin is effective in arresting and exterminating the disease, and provide good grounds for expectation that the results will be permanent.

Dosage and Method of Administration

In all cases penicillin has been given by the intramuscular route only. Sodium penicillin was used for most of the cases, and in recent times the crystalline form whenever obtainable. We also made a trial of the beeswax preparation, but my house-physician at the time found some difficulty in working it, and it was abandoned.

In the early days the total amount given in each course was two million Oxford units (2M). This was soon increased to 3M, and then 4M; and for the last two years the course has been standardized at five million units (5M).

For the first day the doses are small, but thereafter 60,000 units are given every three hours, making nearly half a million units daily, and this rate of administration is continued until a total of approximately five million units has been reached. During the first day, as a precaution against Jarisch–Herxheimer reactions, much smaller doses are given. These may be either of the order of 15,000 units three times in the course of the day, or, as recently, 10,000 units hourly, with orders to the sister to stop administration if the patient seems upset or makes any complaint. No untoward reactions of any kind have been seen.

As will be seen, several of my patients have had repeated courses of penicillin. In the early days we had not appreciated the importance of time as a factor in the improvement of the cerebrospinal fluid and blood; we were not sure enough of our effects, and, dealing with such inexorable conditions as paresis and optic atrophy, we could not afford to take any additional risks. One patient with dementia paralytica had three courses within eight months; another with optic atrophy three courses in 12 months. In the light of subsequent experience such intensity of treatment seems lavish and unnecessary. It is true that the results were very good in both cases, but probably not enough time was given for the full effects of the first course to show themselves, and the same results might now be obtained with more economy of treatment. Gammon, Stokes, *et al.* (1946) suggest that the right time for repetition of the course is after four months, but my experience leads me to think that at that time the whole influence of the first course is not yet apparent either clinically or in the cerebrospinal fluid and blood, and if the clinical condition is satisfactory longer intervals may be allowed.

In several of my cases the cerebrospinal fluid has been examined for evidence of the presence of penicillin, but in no instance has it shown any inhibiting effect on the standard test cultures.

Adjuncts to Penicillin

Of the adjuncts to penicillin the first and most important is time. 5M + 6 months does far more than 5M alone, and in all my more recent cases I have been content to allow intervals of this order before re-examining the cerebrospinal fluid and considering the need for further therapy. Most observers have not given time its opportunity before going on to malaria, but those who have describe very good results.

The second most important adjunct is probably more penicillin. However, until we know the full value of time after the first course it is impossible to say just how valuable a second course is. Effects that were attributed to repetition of the penicillin in Cases 5 and 7 may well have been due in fact to time.

As other adjuncts I have used N.A.B., bismuth, mercurial inunction, and a mercury and iodide mixture in different cases. N.A.B. has been used in three cases in the desire to obtain a negative Wassermann reaction in the blood, since penicillin seemed to have a peculiar weakness in that respect. Mercury and iodide possibly exert a better effect than anything else on the more subacute or chronic pathological formations in meningo-vascular syphilis, and if this is so they have a special place in the treatment.

Tryparsamide I have not as yet used as an adjuvant to penicillin, and until we can assess more exactly the effects of penicillin itself it would be impossible to determine its value in combination, but it obviously may have a place.

Comparison with Malarial Therapy

To revert to the more active of our cases—those with mental symptoms and "paretic" fluids and those with optic atrophy—we have to consider the two burning questions: Are the results as good as those that would have been obtained with malaria?; and, secondly, Could the results be improved by giving malaria as well?

In times past, eight at least, and probably ten, of these patients (including those with optic atrophy) would have received malarial treatment. Would the results have been any better? My own experience says that they would not have been as good, and actually in the last half-dozen cases treated by my colleagues with malaria at Queen Square the serological results to date are not as good as those of the cases treated with penicillin alone. We must bear in mind both the limited effectiveness of malaria and the dangers and difficulties of the treatment. Malaria alone is effective in the sense that it arrests the disease in general paralysis in about 55% of cases, and the remaining cases gradually progress so that 40% of all the patients treated die within five years. The mortality associated with the period of malarial treatment and the subsequent months is 8–10%. The results are considerably improved by combining tryparsamide with malaria, but even with the combination the disease is not arrested in all cases. With penicillin therapy the risks and difficulties of treatment are obviously very much less, and if the results obtained are at all comparable, as they undoubtedly are, the advantages are very conspicuous. I do not overlook the fact that my own small series contains no case of acute G.P.I., but Nicol and Whelan (1947) in this country, and also Smith (1947), have reported great clinical improvement in such cases with penicillin alone.

The American reports are mixed, but Callaway and his associates (1946) considered that treatment with penicillin was more effective than with malaria, and Rose and others (1946) concluded that there was little to choose between the results obtained with penicillin alone and those with malaria followed by tryparsamide. Dattner (1947) considers that penicillin when given in adequate doses is at least as effective in the treatment of neurosyphilis as combined fever and specific chemical therapies. A more detailed account of the American reports has recently been given by Dr. Worster-Drought (1947), and now we have a shorter review by Dr. Nicol (1948).

But there is the further question, Would still better results be obtained by giving malaria as well? Or rather, would any improvement commensurate with the risk be obtained by giving malaria as well? In the last resort this question may be settled by practical experience, and from the reports that have been published of comparable series of cases treated by different methods it is evident that there is no great difference in the results. In a series described by Rose and Solomon (1947) there was no material difference in the percentages of clinical improvement whether the patients were treated with penicillin and malaria, penicillin and the fever cabinet, or penicillin alone. From the report of a smaller series described by Lescher and Richards (1947) in this country it is also evident that the results were very similar, although the observers concluded that the best clinical results seemed to have been achieved with malaria and penicillin, closely followed by those obtained with penicillin alone.

There are two general aims in treatment. The first is to obtain arrest of the disease as rapidly as is possible in consistence with safety, and the second to ensure its permanence. If a rapid arrest can be obtained by any means, additional treatment for the same purpose is useless, and if it involves risk it is certainly unjustified. Treatment cannot

restore the cerebral tissue: it can only arrest the disease. Arrest as rapidly as is consistent with safety is the only first requirement. It seems that the syphilitic processes are inhibited by penicillin before malaria could even come into operation, although further experience is necessary to show whether that inhibition is complete enough in all kinds of cases.

It is fallacious to say that clinical recovery occurs more quickly or more completely after this or that method of treatment, provided only that the treatment is effective—i.e., that it eradicates the disease. After any sufficiently effective treatment the extent of clinical recovery depends on the amount of the cerebral tissue that is capable of recovery, and that is not a function of the treatment but of the viable cerebral tissue. Similarly, the period of clinical recovery is the time required for the recovery of such cerebral tissue as is capable of restored activity. The final results cannot vary between one effective method of treatment and another, provided the treatments themselves are innocuous and reasonably prompt in their actions; and if an effective treatment has once been given no greater or quicker improvement can possibly be obtained by a multiplication of therapies. The practical results that have been reported are in general agreement with this conclusion.

Secondly, to ensure its permanence. Here our only criterion is the serological reactions. After the disease is arrested these take time to become normal, and if the cerebrospinal fluid is of the "inactive" type after three or four months, and normal, apart from the colloidal gold reaction, within a year, we may be satisfied. Such results are obtainable with penicillin as with malaria, and there seems no reason why they should not be as permanent. Though serological relapses must be watched for, they are likely to be few.

Conclusions

As a result of my observations I draw the following conclusions—tentative because longer observation is necessary.

1. Penicillin alone is sufficient in most cases of neurosyphilis. Whether it is adequate for the most acute cases of G.P.I. the experience of this series does not show.

2. If, with the possible exception of such cases, the patient can be kept under observation after treatment and penicillin repeated if necessary, malaria will seldom be called for, and the risk of it will seldom be justified.

3. Even if penicillin does not render malaria unnecessary it is a potent weapon and will make us much less dependent on malaria; and, if malaria is used at all, risks which were necessary before need not now be taken.

BIBLIOGRAPHY

Callaway, J. L., *et al.* (1946). *Amer. J. Syph.*, **30**, 110.
Dattner, B. (1947). *Arch. Neurol. Psychiat.*, **57**, 270.
—— Thomas, E. W., and Wexler, G. (1944). *Management of Neuro-Syphilis.* New York.
Gammon, G. D., Stokes, J. H., and others (1946). *Ann. intern. Med.*, **25**, 412.
Lescher, F. G., and Richards, H. R. M. (1947). *British Medical Journal*, **2**, 565.
Nicol, W. D. (1946). *Brit. J. vener. Dis.*, **22**, 112.
—— (1948). *Post-Grad. med. J.* (Jan.).
—— and Whelan, M. (1947). *Lancet*, **1**, 559.
Rose, A. S., *et al.* (1946). *Arch. Neurol. Psychiat.*, **55**, 428.
—— and Solomon, H. C. (1947). *J. Amer. med. Ass.*, **133**, 5.
Smith, R. H. F. (1947). *Lancet*, **1**, 665.
Worster-Drought, C. (1947). *British Medical Journal*, **2**, 559.

Two settlements in Bethnal Green, Oxford House and University House, are sponsoring schemes for studying social conditions there at first hand. The student is brought into intimate contact with the inhabitants, helping with the shopping or serving behind the counter, and studying the history and geography of the locality. The next course will be held on July 1–28. The fee is 4 guineas, and board and keep at one of the settlements is £2 a week. Further information may be obtained from the Vice-head, Oxford House, Mape Street, Bethnal Green, E.2.

A CASE OF ACUTE PORPHYRIA

BY

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"Acute idiopathic porphyrinuria is clearly recognized in Germany and elsewhere on the Continent; it is being increasingly reported in America, but even to-day it is scarcely mentioned in British literature." The above comment, made in 1939 by Chandler *et al.*, appears as true to-day as it did eight years ago. It has been suggested by clinicians (Rau, personal communication, 1947) who are familiar with the condition that the relatively large number of cases reported in Scandinavia and Germany was primarily due to a more widespread knowledge of the chief features of this rare metabolic disorder. This interest was particularly stimulated by the clinical investigations of Günther (1911), who first described the disease, and by Hans Fischer's elucidation of the chemical nature of porphyrin pigments. The comprehensive reviews of Mason, Courville, and Ziskind (1933) and Dobriner and Rhoads (1940) have recently served to stimulate in America an increased interest in the chemical and clinical aspects of this malady. A brief survey disclosed that no fewer than 36 reports have appeared in the literature in America since 1940, whereas only three indigenous cases have been recorded in British medical journals during the same period. A fourth British case, the chemical aspects of which were fully investigated, was recorded by Prunty (1946) in an American journal.

In man clinical porphyria occurs in the form of two distinct syndromes—congenital porphyria (Garrod, 1923), and acute porphyria.

Congenital Porphyria

This is a very rare disease that develops during foetal life. It is usually recognized in early infancy, and persists in the adult as a permanent disorder of metabolism. Transmission is thought to occur by the inheritance of a gene possessing recessive characteristics (Mackey and Garrod, 1926). Salient features are the excretion of burgundy-coloured urine and a disabling degree of photosensitivity of skin and exposed mucous membranes. Brown pigmentation of bones and pink discoloration of deciduous and permanent teeth have occasionally been recorded (Mackey and Garrod, 1926). Exposure to bright sunlight leads to blistering of unprotected skin and the formation of ulcers, indolent healing of which results in permanent disfiguration by scar tissue. Corneal ulceration due to similar actinic trauma may lead to seriously impaired vision. Both splenomegaly and hepatomegaly have been recorded as transient features in childhood. In this condition excess of uroporphyrin I is excreted.

Acute Porphyria

The symptomatology of this disease, which affects adults, differs entirely from that of the congenital variety. Acute porphyria occurs more frequently in women than in men and the onset is most often during the third decade. It is probable that the symptoms of acute porphyria are merely acute manifestations of a latent chronic metabolic disorder whose asymptomatic phase can be detected only by special investigation of the excreta. The acute and dramatic manifestations of the classical syndrome appear either spontaneously or as a result of prolonged ingestion of certain drugs, of which sulphonal is most commonly incriminated. It thereafter may pursue a prolonged and relapsing course, which often ends fatally. Most recorded cases have been sporadic examples, but recently

an increasing number of reports have indicated that the disease may occur as a familial condition (Nesbitt, 1944). There are factors in the case history recorded below which strongly suggest a familial incidence. It is thought that the inheritance of this disorder is by transmission of a dominant gene (Gates, 1946) whose degree of penetrance is small. Hence this undesirable characteristic may be acquired from a parent who discloses no clinical or metabolic abnormality.

The symptoms of acute porphyria tend to be remarkably stereotyped. The initial attack may be preceded by a prodromal period during which weight is lost and asthenia is pronounced. During this phase various *mental disturbances*—most frequently depression, irritability, or suicidal tendencies—have been notable features. *Abdominal symptoms* follow. There is usually severe para-umbilical colic or lower abdominal cramp-like pain, often associated with nausea and vomiting. Obstinate constipation amounting to a paralytic ileus is constantly present. The abnormal colour of the urine is usually noticed only after the onset of these symptoms, but frequently the significance of this observation is masked by the presence of concomitant icterus. Occasionally patients will admit having excreted dark urine intermittently long before the onset of the illness. A raised blood pressure is a consistent feature at this stage. It is often as high as 180/120, and its discovery in a young adult presenting severe abdominal pain without other localizing features should lead to examination of the urine for porphyrins.

Recovery may occur without further progression of the disease, but relapses are usual, and eventually in about half the cases evidence of *involvement of the central nervous system* appears (Waldenström, 1937). Coma, psychosis, delirium, amaurosis, and epileptic attacks are frequently associated with the more characteristic progressive impairment of motor function. Isolated cranial-nerve palsies, localized weakness of peripheral muscle groups, and more generalized motor involvement develop. Although paraesthesia is usually a marked feature, cutaneous sensibility remains intact. The intensity of the muscular weakness may fluctuate unaccountably, and spread of the paresis to the respiratory muscles, through bulbar involvement, usually terminates the illness. Although photosensitivity and pigmentation of the skin have been recorded in acute porphyria (Nesbitt and Watkins, 1942) they are both regarded as unusual features.

Excessive urinary excretion of uroporphyrin III characterizes most cases of acute porphyria (Waldenström, 1937). On occasion, however, the urinary uroporphyrin III is within normal limits, whereas uroporphyrin I (Prunty, 1946) or coproporphyrin III (Abrahams *et al.*, 1947, Watson *et al.*, 1945) is excreted in excessive amounts.

Case Report

A British soldier aged 26, who had served in the Mediterranean area since 1942, first observed symptoms of ill-health in December, 1946. He noticed that he was lacking in energy, that his limbs, previously very muscular, were now no longer so, and that his uniform had become too loose for him. In spite of increasing weakness, he remained on duty until March 2, 1947, when he was forced to take to his bed with symptoms which were then regarded as being due to "coryza." He was a little better next day and was able to get up, but three days later he was in bed again because of difficulty in standing.

He was admitted to a casualty clearing station seven days after the onset of these acute symptoms. His chief complaints were: central abdominal pain for 24 hours and constipation for three days, a generalized weakness, difficulty in concentration during the day, and sleeplessness at night. It is reported that when first examined at the C.C.S. the patient's condition was extremely poor. He was nauseated and very drowsy; pulse 120, temperature 97° F. (36.1° C.), respirations 20. He was severely dehydrated. The abdomen was distended, epigastric tenderness was present, but there was no rigidity. Liver and spleen were not palpable. The respiratory system was normal, as was the cardiovascular system except that the blood pressure was 140/90. The pupils were constricted, but reacted normally to light and accommodation. All the tendon reflexes were obtainable and the plantar responses were flexor. In spite of obvious muscular wasting, power was good. There was no sensory loss. A generalized superficial lymph-node enlargement was thought to be due to the septic scabies present. The urine contained no sugar or albumin. Total leucocyte count, 22,400 per c.mm. (polymorphs 92%, lymphocytes 3%, monocytes 5%).

On re-examination the following morning a generalized pigmentation of the skin was noticed. The knee- and ankle-jerks and abdominal reflexes were now unobtainable. The left plantar response was equivocal. Lumbar puncture was performed. The pressure was normal and the fluid clear. Protein amounted to 35 mg. per 100 ml. There was no excess of globulin.

During the next few days the patient's condition, which remained critical, showed little change. Slight icterus of the conjunctiva was noticed on March 12.

On March 18 he was transferred to a British general hospital. The pulse was now 104, temperature 97° F., respirations 25, blood pressure 150/100. Lethargy was still marked, but the patient responded rationally to interrogation. Loss of power in all limbs was noted for the first time. All tendon reflexes were present except for the Achilles jerk. Plantar responses were both equivocal. There was no loss of cutaneous sensibility. The intense brown pigmentation of the skin was again a subject of comment, and it was suggested that it might be of pellagrous origin. With this in mind, and with the intention of demonstrating the associated excess porphyrin, two specimens of urine were allowed to stand exposed to the light for 24 hours, but no deepening of colour was observed. Owing to subsequent lack of response to nicotinic acid therapy, no further investigations into this aspect of the problem were made, nor were any pigmentary abnormalities detected during further routine laboratory examinations of the urine. By mid-April the gradually increasing weakness had proceeded to a stage in which limb movements were almost completely absent. Speech was slurred, but there was no dysphagia. The corneal reflexes were absent, as were all tendon reflexes, although cutaneous sensation was still unimpaired. Muscles were slightly tender to pressure. Lumbar puncture was repeated. Pressure was normal; protein totalled 70 mg. per 100 ml. with excess globulin; and there were 2 cells per c.mm. By this time an extensive series of investigations had been completed. Radiographs of the chest, repeated cultures of blood, urine, faeces, and throat, blood examinations for malaria parasites, and serum agglutinins disclosed no abnormality. Fasting blood sugar was 140 mg. per 100 ml., blood urea 90 mg. per 100 ml., serum protein 5.8 g. per 100 ml., van den Bergh reaction negative, haemoglobin 95%, and E.S.R. 32 mm. in 1 hour.

At this stage 10 ml. of "eucortone" was administered each day without any therapeutic response. "Prostigmin," 0.5 mg. intramuscularly three times a day, was equally ineffective in relieving the profound asthenia. During the first few days of April the patient remained extremely feeble. There was incontinence of faeces and urine; drowsiness during the day was increasing, whereas insomnia at night remained a troublesome feature in spite of sedation with barbiturates. At times attacks of tachycardia and breathlessness occurred. A slight improvement began in the second week of May, and his condition, although still very serious, permitted transfer to England.

The patient was admitted to Redhill County Hospital on May 18. He was a mentally alert individual showing very severe emaciation and extreme loss of muscle substance. The most striking feature, however, was a dusky pigmentation, which was most marked on the face but was also present on the arms and thorax, and to a less extent on the abdomen and legs. The hair was dark brown. (It was later established that his complexion had always been fair, and that when on leave in November, 1946, the dark colour of his hair and pigmented features had astounded his relatives.) The skin was scaly, and lesions of scabies were still present. There were hyperkeratotic patches on the flexor aspects of the fingers and on the palms and soles.

Central Nervous System.—Mentality normal. Amnesic for events occurring during early part of illness. Not aphasic, but could articulate only in a whisper. Pupils unequal, right larger than left; both reacting normally to light and accommodation. Fundi normal except that the arteries and veins were abnormally constricted. Eye movements were full and visual fields normal. No nystagmus. The muscles of mastication were of normal power. Extreme weakness present in all facial muscles, particularly frontales and orbiculares oculi, so that the cornea was always exposed, even during sleep. There was severe conjunctivitis and keratitis of both eyes. The palate moved normally and there was no dysphagia. The tongue, which was normally protruded, was wasted and deeply furrowed, with coarse fasciculation evident. Sensation of taste was not impaired. The right vocal cord moved normally, the left very sluggishly. The cervical muscles were of fair power, and the intercostal and diaphragmatic movements of normal range. All four limbs were flaccid and lay in positions dictated by gravity. There were weak movements of finger flexion in the left hand only. Except for ineffectual contractions of the upper fibres of both pectorales major, the muscles activating the shoulder-, elbow-, and wrist-joints were completely paralysed. The lower limbs retained fair power in the glutei, tensores fasciae latae, hamstrings, and posterior tibial muscles. Contractility of the quadriceps femoris, which were barely palpable as thin straps on the femur, was absent. Anterior tibial and peroneal groups likewise were totally paralysed. There was fair power of flexion of the toes. The deep and superficial reflexes were all unobtainable. The plantar responses, in the absence of contractility of the extensors of the toes, were necessarily flexor. There was no fibrillation of muscles other than the tongue. Complete faecal incontinence, but normal bladder control, was present. There was no sensory loss.

The pulse was regular 96, the blood pressure 110/80, and heart normal. There was no abnormality in the respiratory system. The liver and spleen were not palpable. The descending colon was palpable and spastic.

Investigations.—The combinations of inaugural abdominal symptoms with cerebral disturbances, evidence of lower-motor-neurone paresis, and cutaneous pigmentation led to the examination of the urine for porphyrins. Spectroscopic investigation of a freshly passed specimen showed the typical double band of the zinc-porphyrin complex (Chandler *et al.*, 1939). Ehrlich's benzaldehyde test (Jorgensen and With, 1947) before and after extraction of the urine with acid ether was positive, indicating the presence of porphobilinogen. An amyl alcohol extract of the urine displayed intense pink fluorescence when exposed to Wood's light, as did a specimen of faeces. Urine when first voided was the colour of sherry, and on standing it assumed a dark coffee colour in 24 to 48 hours.

Further investigations resulted as follows: haemoglobin, 94%; R.B.C., 4,500,000; colour index, 1.04; leucocytes, 8,000 per c.mm. (polymorphs 34%, lymphocytes 55%, monocytes 4%, eosinophils 7%); blood urea, 68 mg., fasting blood sugar 94 mg. and blood cholesterol 124 mg. per 100 ml., Kahn, trace; Wassermann ±; Laughlen ±. Total plasma protein, 5.25 g.% (albumin 2.8 g., globulin 2.45 g.), chloride 343 mg., potassium 18.4 mg., and sodium 321 mg. per 100 ml., carbon-dioxide-combining power, 57 vols.%; serum bilirubin, 0.4 mg. per 100 ml. Thymol turbidity test, negative. Alkaline phosphatase, 2.4 Bodanski units. Cerebrospinal fluid: pressure normal; protein, 50 mg. per 100 ml.; Pandy, trace; chlorides, 680 mg. per 100 ml.; lymphocytes 1 per c.mm.; W.R. negative; Benzoin reaction, 00000. The electrocardiogram was normal. Sternal-marrow examination showed normoblastic haemopoiesis with evidence of hypoplasia of erythroblastic elements. The white-cell development was normal. Exposure to bright July sunlight resulted within 45 seconds in an intense irritation of the skin and marked erythema, both of which persisted for an hour. Test exposure to a mercury-vapour ultra-violet lamp for half an erythema dose had no effect.

Family History.—The patient's mother stated that she had never noticed any urinary abnormality in herself or in her children. She had never experienced attacks of colic. The father had died of pneumonia at the age of 29. The maternal grandfather, who had been a painter by occupation, died at 25. It was reported to me that the cause of death was "painter's colic." One sister, two stepsisters, and a stepbrother were healthy, as was the patient's son, aged 6 years. An attempt to investigate the urine of these individuals met with formidable opposition. Nevertheless specimens were obtained from the patient's son, mother, and sister. No abnormal pigments were detected in the urine of the son and mother, but that of the sister was deeply coloured, darkened slightly on standing, and reacted positively with Ehrlich's benzaldehyde reagent after ether extraction, indicating the presence of porphobilinogen. Schlesinger's test on the same specimen was negative.

Progress.—During the two months that the patient remained at Redhill County Hospital there was a slow but steady improvement in his state of nutrition, and his sleep habit rapidly reverted to normal rhythm. Except for return of contractility, so slight as to be ineffective, in muscles which previously had been quite inert, increase of muscle power did not occur. There was a considerable decrease in the depth of colour of the urine when first passed, and the final depth after standing was less than it had been on admission, but the spectral bands did not indicate that any reduction of porphyrin excretion was occurring. The improvement noted appeared to be independent of the treatment given, which consisted in the seriatim intramuscular administration of liver preparations, folic acid, and calcium gluconate.

Five 24-hour specimens of urine were collected between June 15 and 19 and submitted to Prof. C. Rimington, who confirmed the presence of excess porphyrin and identified it as uroporphyrin III. Coproporphyrin was present in normal amounts. The excretion of uroporphyrin on the five days was 9.7, 9.4, 8.6, 8.3, and 9.5 mg. respectively. The patient was transferred to an E.M.S. hospital near his home on July 14. A progress report from that hospital stated that a relapse had recently occurred, during which power in all muscles, except those innervated by the cranial nerves and those subserving respiration, was quite absent. Colic and nausea were again conspicuous features, as was a marked hypotension, the latter responding to eucortone.

Comment

This case, which presented many of the typical features of acute porphyria, illustrated particularly clearly the nature of the diagnostic problem confronting the clinician when neurological symptoms and signs are pre-eminent. When abdominal symptoms predominate, as they often do, errors in diagnosis have led to injudicious laparotomy. The difficulties in the differential diagnosis of these rare cases presenting a tangle of features referable to many of the bodily systems may be totally resolved by the discovery of abnormal pigments in the urine. Nesbitt (1944) states that "the diagnosis of acute porphyria will be made only if it is borne in mind." The view that acute porphyria is an inborn familial metabolic disorder is supported by the evidence in the above case.

It is thought probable that the grandfather's fatal illness was acute porphyria and not "painter's colic," which it may closely simulate. Porphobilinogen was demonstrated in the urine of the apparently healthy sister, emphasizing that it is important to search for latent porphyria among relatives of the acute case. These individuals should be warned not to take drugs which have been known to precipitate the acute condition. According to Dobriner and Rhoads (1940) the following drugs are suspect: sulphonal, "trional," sulphonamides, barbiturates, arsenicals, alcohol, phosphorus, selenium, and lead. It is noteworthy that, although there is no direct evidence of any causal relationship, mepacrine had been taken by the patient as a malaria prophylactic during the previous three summers. His critical condition prevented investigation of the effect of a provocative dose of this drug.

Although pigmentation and photosensitivity were marked features of this case, both of these effects are rare in acute porphyria (Mason, Courville, and Ziskind, 1933).

Summary

An example of acute porphyria occurring in a young man is described. Abdominal and mental symptoms and neurological signs were present. Pigmentation and photosensitivity were conspicuous features. There was some evidence of a familial distribution of the disease.

I am indebted to Dr. G. H. Jennings for his encouragement and permission to publish this report; to Prof. C. Rimington for his kindness in performing the assays; to the R.A.M.C. officers whose notes furnished the basis of the early part of the case history; and to Miss E. W. M. Johnson for her help with the biochemical investigations.

REFERENCES

Abrahams, A., Gavey, C. J., and Maclagan, N. F. (1947). *British Medical Journal*, **2**, 327.
Chandler, F. G., Harrison, G. A., and Rimington, C. (1939). Ibid., **2**, 1173.
Dobriner, K., and Rhoads, C. P. (1940). *Physiol. Rev.*, **20**, 416.
Garrod, A. E. (1923). *Inborn Errors of Metabolism*. London.
Gates, R. R. (1946). *Human Genetics*. New York.
Günther, H. (1911). *Disch. Arch. klin. Med.*, **105**, 89.
Jorgensen, J., and With, T. K. (1947). *Lancet*, **1**, 54.
Mackey, L., and Garrod, A. E. (1926). *Quart. J. Med.*, **19**, 357.
Mason, V. R., Courville, C., and Ziskind, E. (1933). *Medicine*, **12**, 355.
Nesbitt, S. (1944). *J. Amer. med. Ass.*, **124**, 286.
—— and Watkins, C. H. (1942). *Amer. J. med. Sci.*, **203**, 74.
Prunty, F. T. G. (1946). *Arch. intern. Med.*, **77**, 623.
Waldenström, J. (1937). *Acta med. scand.*, Suppl. 82.
Watson, C. J., Schwartz, S., and Hawkinson, V. (1945). *J. biol. Chem.*, **157**, 345.

A CASE OF ACUTE MONONITROBENZENE POISONING

BY

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Mononitrobenzene, or oil of mirbane, is a yellow oily liquid which on account of its strong smell is also known as "artificial essence of bitter almonds." Since it was first prepared early in the nineteenth century many cases of poisoning with this substance have been recorded—by absorption through the skin, by inhalation, or when taken by mouth.

Poisoning by skin absorption has followed the use of soap scented with it (Nicholson, 1862), spilling the fluid on the clothes (Loeb, Bock, and Fitz, 1921; Hamilton, 1919–20; Letheby, 1863–4), or application to the hair of anti-louse preparations made with it (Wolpe, 1920; Bohland, 1919; Schultz, 1915). Shoe dyes often contain nitrobenzene as a solvent, and the wearing of recently dyed shoes before they are properly dry has led to many cases of poisoning. Muehlberger (1925) has reviewed the literature on this subject and pointed out that aniline is the solvent most commonly employed, and may give rise to similar symptoms. Levin (1931) has reported a case of orthotoluidine poisoning caused in the same way. Marking-ink also may be prepared with nitrobenzene or aniline, and babies seem to be very easily affected by newly marked napkins: Rayner (1886) first reported a series due to aniline, and Ewer (1920) and Thomsen (1921) have reported cases due to nitrobenzene. In many of these episodes inhalation may have contributed to the intoxication: acute poisoning due to inhalation alone is relatively infrequent, but Stevenson and Forbes (1942) and Stevens (1928) have reported cases following the use of nitrobenzene in bed-bug exterminators.

Poisoning by ingestion has occurred in numerous ways. The majority of cases are accidental, either errors in dispensing (Carter, 1936; Leader, 1932; Thomas, 1926) or mistakes by patients as reported by Chapman and Fox (1945), where furniture polish containing nitrobenzene was taken instead of an alkaline stomach mixture. Hogarth (1912) published a case following the rubbing of nitrobenzene on the gums as an anodyne for toothache. Other cases have arisen from taking alcoholic drinks which have been contaminated with the substance (Loeb, Bock, and Fitz, 1921; Scott and Hanzlik, 1920) or from drinking a nitrobenzene preparation when intoxicated (Adler, 1934; Wandel, 1919). Food contaminated with the liquid is a rare cause (Hilbert, 1915), though Taylor (1864) reported the case of a woman who tasted the flavouring she was going to use in some pastry and developed nitrobenzene poisoning. Curiosity on the part of children accounts for some cases (Nobécourt and Pichon, 1924); a few are suicidal (Fullerton, 1930; Schild, 1895); and on many occasions the liquid has been taken as an abortifacient, usually without success (Güntz, 1930; Schnopfhagen, 1927; Spinner, 1917; Schild, 1895).

Chronic poisoning is usually industrial. Workers in aniline plants may develop symptoms from nitrobenzene inhalation; it is less common than aniline intoxication, but is more dangerous when it does occur. Engel (1934), Balsac *et al.* (1930), Hamilton (1919–20, 1921), and Letheby (1863–4) have discussed industrial nitrobenzene poisoning, and Adams (1912) has described an unusual case of non-industrial chronic intoxication.

Case Report

The patient, a Polish girl aged 19, was admitted to University College Hospital on July 23, 1947. About three months previously, while she was in Germany as a displaced person, she had married an English soldier, who brought her to London and left her with her mother-in-law while he returned to his unit. She did not get on very well in her new home, and partly out of curiosity and partly, one suspected, hoping to get her husband repatriated she decided to taste the fluid in a bottle labelled "poison." This bottle had been bought by her late father-in-law many years previously and was lying about the house; her husband had warned her that it was poisonous and forbidden her ever to touch it. About 6.30 p.m. on July 22 she poured some of the fluid into a glass and sipped it; she felt nauseated, and vomited several times during the night. The next morning she was seen to be blue, and was therefore sent to hospital.

When seen at 3 p.m. on July 23 she was fully conscious and well orientated. She showed "blue-grey" cyanosis and was vomiting repeatedly, the vomit being bright yellow but without smell. She was afebrile; pulse rate 90; respiration was of normal depth and rate, but the breath smelt strongly of almond essence. Physical examination revealed no other abnormalities. The urine was dark in colour and became darker on standing; it contained a trace of albumin and did not reduce Benedict's reagent.

The stomach was washed out with saline, after which the vomiting ceased. Oxygen inhalations failed to affect the cyanosis, and blood withdrawn from a vein was brownish in colour and shown to contain methaemoglobin. 20 ml. of 0.5% solution of methylene blue was injected intravenously and within 30 minutes the patient's colour was restored to normal.

The next day (July 24) her breath still smelt of almond essence and continued to do so until July 27. The cyanosis was then nearly as deep as before the injection of methylene blue, but it did not seem to be inconveniencing the patient. Oral methylene blue, 2 gr. (130 mg.) four-hourly, was given for two days, and subsequently ascorbic acid, 100 mg. four-hourly, but neither of these seemed to accelerate the disappearance of the cyanosis, which ceased to be detectable on July 29. The urine on July 25 was of normal colour, but still contained a trace of albumin.

On July 29 it was observed that the patient was faintly icteric, and that a severe haemolytic anaemia was developing (see Chart). On July 30 and 31 she passed urine that was almost black, and spectroscopic examination showed that it contained haemoglobin and methylene blue; a sample of plasma on the latter date contained methaemalbumin and haemoglobin. Red cell fragility showed haemolysis starting at 0.48% saline and complete at 0.28%, and a blood film revealed very marked anisocytosis, polychromasia, punctate basophilia, and six

nucleated red cells per 100 white cells. By July 31 her blood pressure had fallen from its initial level of 110/85 to 98/50 and her pulse rate had risen to 104; it was therefore decided to give a transfusion of 2 pints (1.36 litres) of blood. Her condition subsequently improved rapidly, and she left hospital on Aug. 8. When seen on Aug. 25 she had no symptoms.

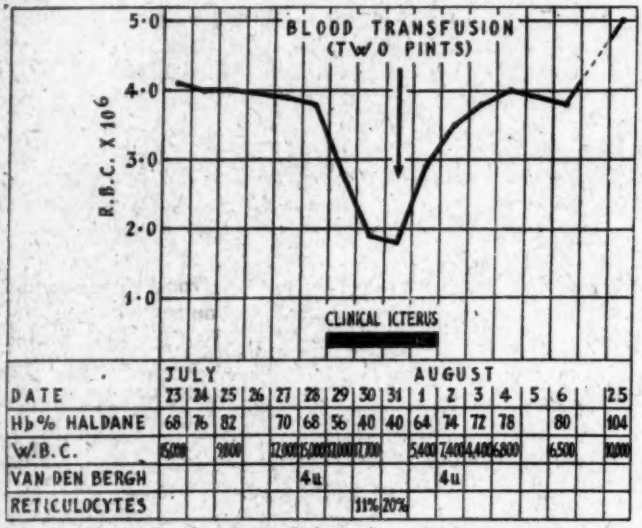

Chart showing haemolytic action of nitrobenzene.

The bottle from which the fluid was taken contained a yellow oily liquid smelling strongly of almond essence and rather indistinctly labelled "nitrobenzene." That the bottle contained nitrobenzene was subsequently confirmed chemically. It was impossible to ascertain the purpose for which it had originally been obtained.

Discussion

Nausea and vomiting are the first symptoms after the oral ingestion of nitrobenzene; they develop within a few minutes, and are followed in from one to twelve hours by the appearance of cyanosis and in severe cases by neurological symptoms. In cases of poisoning by skin absorption or inhalation the cyanosis develops more rapidly. It is now generally considered that the cyanosis is due to the development of methaemoglobin in the red blood cells, although many earlier investigators—for example, Loeb, Bock, and Fitz (1921)—were unable to detect methaemoglobin in the blood, and postulated the development of a nitrobenzene haemoglobin compound. Hamblin and Mangelsdorff (1938) devised a recording spectrophotometer and used this to detect methaemoglobin, which they found in the blood in all cases of nitrobenzene poisoning in amounts proportional to the clinical condition and cyanosis.

The neurological symptoms that may be seen in the early stages are progressive drowsiness leading to coma and in fatal cases respiratory paralysis. These have been attributed either to a direct toxic action of the poison on the central nervous system or to anoxaemia. Loeb, Bock, and Fitz (1921) reported the case of an unconscious patient with a blood-oxygen-carrying capacity of 6.2 volumes % who recovered consciousness on being given a blood transfusion: although cases have been reported showing spontaneous recovery from nitrobenzene coma (Güntz, 1930), it is suggestive that in this case recovery was due to improved oxygenation following the transfusion. Steele and Spink (1933) report a case of aniline poisoning with cyanosis and coma in which recovery of consciousness followed the intravenous administration of methylene blue, which converted the methaemoglobin to haemoglobin and restored the oxygen-carrying capacity of the blood. However, Levin (1927), in investigations of the effect of nitrobenzene on animals, found that, whereas dogs, cats, and rats developed cyanosis and neurological symptoms, rabbits and guinea-pigs failed to develop cyanosis but nevertheless died. It appears therefore that, although anoxaemia may play a part in the production of neurological symptoms and death, a direct toxic action on the nervous system is an important factor.

In all moderately severe cases of nitrobenzene poisoning some haemolysis is found, starting about the fifth or sixth day. Engel (1934) mentions that the haemoglobin level may fall to 30%; Leinoff (1936) records a case in which it was 45%. Clinical icterus is present when haemolysis is severe and the spleen occasionally becomes palpable (Hilbert, 1915; Schild, 1895). The process is usually self-limiting, and blood transfusion is not often required.

Late sequelae are unusual in cases of acute poisoning, although Adler (1934) reported a case in which a neurological disturbance suggesting a lesion of the basal ganglia followed four days' unconsciousness due to nitrobenzene; and Grafe and Homburger (1914) reported a case in which mental deterioration was a sequel. It is possible that in the first case prolonged cerebral anoxia was an important factor.

Laboratory Investigations

In the early stages spectroscopic examination of the blood is useful in confirming the presence of methaemoglobin. A daily red cell count is advisable to ascertain the severity of the haemolytic process. Haemoglobin estimations are satisfactory if done by the Sahli method, but in this case only that of Haldane was available, and although the results are recorded in the Chart the presence of methaemoglobin makes them unreliable. The white blood cells may show a polymorphonuclear leucocytosis in the early stages, and Loeb, Bock, and Fitz (1921) report 40,000 per c.mm. in one case; a second rise during the haemolytic phase may also be found.

The urine initially may be dark, especially on standing; this has been noted on many occasions, and, according to Loeb, Bock, and Fitz (1921) and to Meyer-München (1905), is due to nitrobenzene being excreted as para-amidophenol. It is often said that the urine may contain a reducing substance, but this is rarely reported in case summaries, although Wolpe (1920) stated that one of his patients had 0.1% sugar in the urine the day after poisoning (method of testing not mentioned). Engel (1934) attributes this property of the urine to the presence of glycuronic acid, with which para-amidophenol is conjugated for excretion. The passage of dark urine in the haemolytic phase is unusual, although Güntz (1930) mentions it in his case.

Treatment

The recognition of acute nitrobenzene poisoning should not be difficult with the extreme cyanosis and characteristic smell, and if the history suggests oral ingestion the stomach should be washed out. If the patient is unconscious, steps should be taken to restore the oxygen-carrying capacity of the blood, a procedure which may terminate the coma although it will not affect the direct toxic action on the nervous system. Blood transfusion and replacement transfusion have both been used with good results: Chapman and Fox (1945) had a patient in semicoma who was much improved by venesection and transfusion of 3 pints (1.7 litres) of blood. In view of the ability of methylene blue to convert methaemoglobin to haemoglobin, such measures would seem to be unnecessary, although in the case of replacement transfusion it has the theoretical advantage of reducing the amount of poison acting on the nervous system. Methylene blue was first advocated as a result of animal experiments for use in cyanide and carbon monoxide poisoning. In the latter it was considered to improve cell metabolism, whereas in the former it was thought to convert

haemoglobin to methaemoglobin, which fixed the cyanide and prevented its toxic action (Wendel, 1933). However, despite this evidence, Steele and Spink (1933) used methylene blue in two cases of aniline poisoning with dramatic disappearance of methaemoglobinaemia, and Williams and Challis (1933) in one case. Subsequently Wendel (1937) agreed that it had this action in man in the dose used; and Hartman, Perley, and Barnett (1938) made a detailed study of it as an antidote for methaemoglobinaemia following sulphonamide therapy. Only two reports have been found of its use in nitrobenzene poisoning: Walterskirchen (1939) employed an unstated amount of 1% solution of methylene blue intravenously, and the cyanosis cleared in 15 minutes; and Leinoff (1936) gave 50 ml. of a 1% solution intravenously, and describes the patient as at first becoming darker blue, then within one hour the condition improved and the finger-nails became pink. He does not mention a return of the cyanosis, but this is implied in the subsequent statement that it disappeared completely in a few days. The dose given in the case reported here is much smaller than that advised by Hartman *et al.* (1938)—1–1.5 mg. per kg. The subsequent oral administration had less effect than would have been expected in view of the finding of the same workers that 1–2 gr. (0.065–0.13 g.) four-hourly controlled sulphonamide cyanosis. The use of ascorbic acid was suggested by Deeny, Murdock, and Rogan (1943), who reported on its use in congenital methaemoglobinaemia, and by Carnrick, Polis, and Klein (1946) in the acquired type, although in this case it was really given too late to say whether it was beneficial.

There does not seem to be any danger in giving methylene blue in these doses, although coloration of the urine may surprise the patient and injection outside the vein may cause a severe and painful inflammatory reaction.

Subsequently the extent of the haemolytic process must be watched, and, if the haematological or clinical condition demands it, blood transfusion should be given. In the present case it is probable that the haemolysis was maximal at the time of the transfusion and that the condition would have improved satisfactorily without it.

Summary

A case of acute nitrobenzene poisoning following oral ingestion is reported. Cyanosis and haemolytic anaemia were the outstanding clinical features. Methylene blue was used in the treatment of the methaemoglobinaemia, and the haemolytic anaemia was so severe as to need a blood transfusion.

I have to thank Dr. F. M. R. Walshe for permission to publish this case, and Dr. M. Maizels, Dr. M. E. Morgans, Dr. E. Roderic-Evans, and Mrs. C. E. Work for the investigations.

References

Adams, S. S. (1912). *Trans. Ass. Amer. Phys.*, **27**, 503.
Adler, A. (1934). *Z. ges. Neurol. Psychiat.*, **150**, 341.
Balsac, F. Heim de, Agasse-Lafont, E., and Feil, A. (1930). *Progr. méd., Paris*, **57**, 817.
Bohland, K. (1919). *Dtsch. med. Wschr.*, **45**, 1388.
Carnrick, M., Polis, B. D., and Klein, T. (1946). *Arch. intern. Med.*, **78**, 298.
Carter, F. W. (1936). *Med. J. Aust.*, **2**, 558.
Chapman, W. M., and Fox, C. G. (1945). *British Medical Journal*, **1**, 557.
Deeny, J., Murdock, E. T., and Rogan, J. J. (1943). Ibid., **1**, 721.
Engel, H. (1934). *Occup. & Hlth*, **2**, 334 (No. 286). Geneva.
Ewer, H. (1920). *Dtsch. med. Wschr.*, **46**, 1078.
Fullerton, W. W. (1930). *New Engl. J. Med.*, **203**, 423.
Grafe, E., and Homburger, A. (1914). *Z. ges. Neurol. Psychiat.*, **25**, 343.
Güntz, E. (1930). *Dtsch. Z. ges. gerichtl. Med.*, **15**, 461.
Hamblin, D. O., and Mangelsdorff, A. F. (1938). *J. industr. Hyg.*, **20**, 523.
Hamilton, A. (1919–20). Ibid., **1**, 200.
—— (1921). U.S. Department of Labour, Bureau of Labour Statistics, *Bulletin*, No. 280.
Hartman, A. F., Perley, A. M., and Barnett, H. L. (1938). *J. clin. Invest.*, **17**, 699.
Hilbert (1915). *Dtsch. med. Wschr.*, **41**, 1115.
Hogarth, C. W. (1912). *British Medical Journal*, **1**, 183.
Leader, S. D. (1932). *Arch. Pediat.*, **49**, 245.
Leinoff, H. D. (1936). *New Engl. J. Med.*, **215**, 191.
Letheby, H. (1863–4). *Pharm. J. Trans.*, **5**, 2nd ser., 130.
Levin, S. J. (1927). *J. Amer. med. Ass.*, **89**, 2178.
—— (1931). Ibid., **96**, 681.
Loeb, R. F., Bock, A. V., and Fitz, R. (1921). *Amer. J. med. Sci.*, **161**, 539.
Meyer-München, E. (1905). *Berl. klin. Wschr.*, **42**, 1353.
Muehlberger, C. W. (1925). *J. Amer. med. Ass.*, **84**, 1987.
Nicholson, E. (1862). *Lancet*, **1**, 135.
Nobécourt and Pichon, E. (1924). *Paris méd.*, **53**, 380.
Rayner, W. (1886). *British Medical Journal*, **1**, 294.
Schild, W. (1895). *Berl. klin. Wschr.*, **32**, 187.
Schnopfhagen, H. (1927). *Wien. klin. Wschr.*, **40**, 998.
Schultz (1915). *Münch. med. Wschr.*, **62**, 458.
Scott, R. W., and Hanzlik, P. J. (1920). *J. Amer. med. Ass.*, **74**, 1000.
Spinner, J. R. (1917). *KorrespBl. schweiz. Arz.*, **47**, 1439. Abstract in *J. Amer. med. Ass.*, **69**, 2155.
Steele, C. W., and Spink, W. W. (1933). *New Engl. J. Med.*, **208**, 1152.
Stevens, A. M. (1928). *J. Amer. med. Ass.*, **90**, 116.
Stevenson, A., and Forbes, R. P. (1942). *J. Pediat.*, **21**, 224.
Taylor, A. S. (1864). *Guy's Hosp. Rep.*, **10**, 193.
Thomas, D. R. (1926). *Indian med. Gaz.*, **61**, 229.
Thomsen (1921). *Münch. med. Wschr.*, **68**, 399.
Walterskirchen, L. (1939). *Wien. klin. Wschr.*, **52**, 317.
Wandel (1919). *Münch. med. Wschr.*, **66**, 1267.
Wendel, W. B. (1933). *J. Amer. med. Ass.*, **100**, 1054.
—— (1937). Ibid., **109**, 1216.
Williams, J. R., and Challis, F. E. (1933). *J. Lab. clin. Med.*, **19**, 166.
Wolpe, L. (1920). *Dtsch. med. Wschr.*, **46**, 100.

HETEROTOPIC OSSIFICATION OF AN APPENDICULAR MUCOCELE

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By the term "heterotopic ossification" is meant the appearance of osseous tissue in an organ which has no ontogenetic relationship to the process of ossification. The spontaneous occurrence of heterotopic ossification has been observed in the most unexpected tissues and organs, as, for example, aneurysmal walls, old haematomata, laparotomy scars, injured muscles and nerves (Leriche and Policard, 1926), arterial walls (Mönckeberg, 1902), tonsils (Reitmann, 1903), aortic valves (Rosenstein, 1900), the anterior chambers of the eyes (Koch *et al.*, 1939), tissues affected by elephantiasis (Kleine, 1929), and of course tumours (Leriche and Policard, 1926; Törö, 1935).

Experimentally, the condition has been obtained by ligation of the renal vessels, in granulation tissue by a variety of methods (Leriche and Policard, 1926), by grafting a portion of gall-bladder mucosa, urinary-bladder mucosa, or even gastric mucosa into various connective tissues (Cavalli, 1939; Jung and Cemil, 1935; Leriche and Lucinesco, 1935; Lucinesco and Cavalli, 1935, 1936; Santa and Marcacci, 1938), or when a portion of an aponeurosis has been used to replace a defect in the urinary bladder wall (Neuhof, 1918-20; Huggins, 1931; Phemister; Copher and Key).

The mechanism of heterotopic ossification is still a matter of controversy. Conheim supported the theory of latent embryonic points of ossification; Ollier that of periosteal displacements; Busch, Macewen, and Ribbert that of the haematogenous seeding of osteoblasts. At present the hypothesis of Leriche and Policard is favoured —namely, that the principal requirements for the occurrence

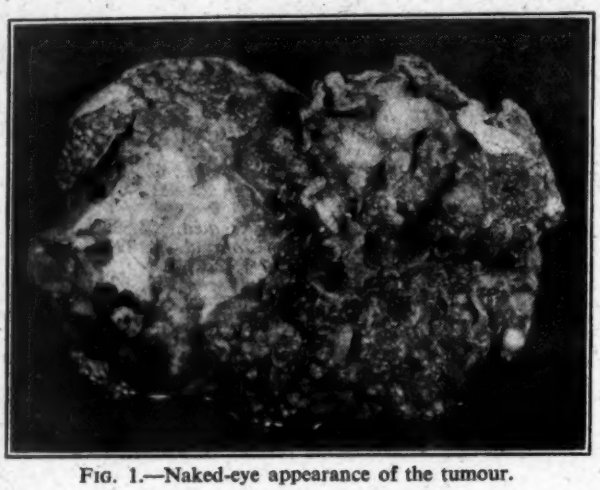

FIG. 1.—Naked-eye appearance of the tumour.

of heterotopic ossification are the creation of a granulation tissue and the deposit therein of calcium salts, these processes occurring either together or in succession.

Slowing down of the circulation, produced by venous stasis, is a factor in fibrous ossification. Ischaemia is a factor in enchondral ossification (Giuliani, 1934).

Our present work deals with a case of heterotopic ossification of a mucocele of the vermiform appendix. This had opened into the peritoneal cavity and was associated with a gelatinous condition of the peritoneum (Péan's disease or Werth's pseudo-mycomatosa peritonealis). The appendix was located in the sac of an inguinal hernia. The condition was discovered at an emergency operation for strangulation of the hernia.

Case Record

The patient, a man aged 70, was admitted to hospital on the afternoon of May 14, 1946, with strangulation of a right inguino-scrotal hernia. The hernia first appeared six years before and had since strangulated twice. On each occasion reduction of the hernia was successfully carried out after one or two hours. On May 14, immediately after a muscular effort, strangulation recurred, and repeated attempts by the patient to reduce the hernia were unsuccessful. He was admitted six hours after the onset of strangulation. On admission his general condition was found to be good. The bowels had moved, and an irreducible hard inguino-scrotal tumour was found on the right side.

Operation (Radical cure. Spinal "percaine" and ephedrine).—The sac was dissected out and the contents found to be stony hard. On opening the sac an osseous body about 7 cm. long was found, bound to the omentum at its upper pole. With a view to determining the nature of this tumour the incision was extended superiorly and the abdomen opened, whereupon a large quantity of mucus flowed out through the abdominal incision. A gelatinous condition of the peritoneum secondary to rupture of an appendicular or other mucocele was suspected and the caeco-appendicular area was explored.

FIG. 2.—From above downwards: smooth-muscle tissue with fragments of epithelium; granulation tissue, with areas of calcification; osseous tissue. (Mann's stain; ocular × 5; objective No. 3, Zeiss.)

The osseous body was found to be in direct connexion with a remnant of the appendix, approximately 1 cm. in length. The tumour and the appendicular remnant were removed and the operation finished by the method of Bassini.

Post-operative progress was normal and the patient was discharged after 12 days. A general examination of the patient six months later was satisfactory.

Pathological Examination of the Tumour.—The tumour (Fig. 1) was ellipsoidal in shape, about 7 cm. in length, opaque to *x* rays, and covered by soft tissues only over its upper pole. Microscopically it was seen to be a terminal atrophic portion of a vermiform appendix, with a tendency to sclerosis. The principal mass of the tumour consisted of three main histological elements—epithelium, granulation tissue, and osseous tissue (Fig. 2). The epithelium was of intestinal type and showed areas of hypertrophy and hyperplasia as well as of atrophy. These epithelial areas occurred in islands or in long strands. In some areas there were smooth-muscle fibres in relation to the epithelium. The lumen of the appendix, where it was still visible, was filled with an amorphous material which took up a rose-red colour when stained with Mayer's mucicarmine. The granulation tissue was situated between the epithelium and the osseous tissue. It showed areas of necrosis near the epithelium and of calcification near the osseous tissue. It could be clearly seen that calcium salts were being deposited in the necrotic areas, and that ossification was occurring in the calcified zones, where osteoblasts penetrated through connective-tissue trabeculae (Fig. 3). Peripherally the osseous tissue was contiguous with and external to the calcified zones. It contained typical bone

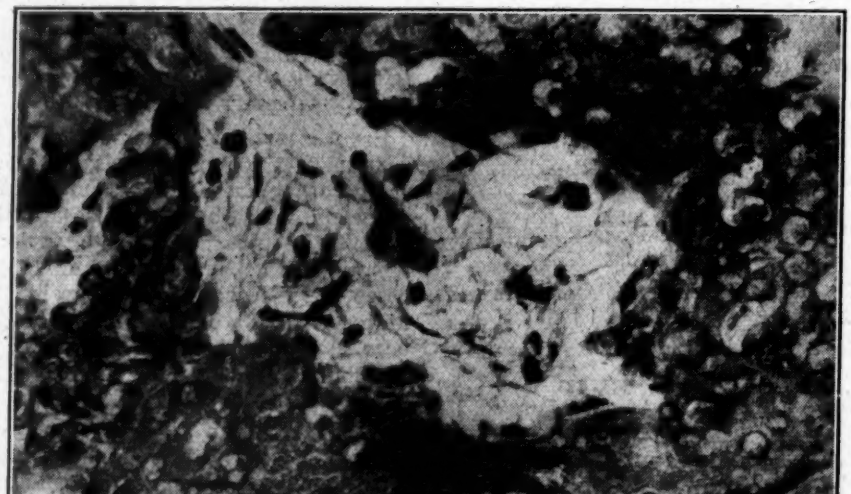

FIG. 3.—For description, see text. (Giemsa stain; Oil-immersion objective No. 60, Zeiss.)

cells and medullary spaces having blood capillaries and scanty haemopoietic cells. The direction of the Sharpey fibres showed clearly that the osseous tissue had been subjected to continual mechanical stress.

Discussion

In retrospect the condition is considered to have been a perforated appendicular mucocele (in the sense used by Ferret in 1876) for the following reasons. There was a gelatinous condition of the peritoneum, and the pedicle of the tumour consisted of an appendicular remnant. On section the tumour showed portions of intestinal epithelium and mucous cavities.

The case can be considered to be a fortuitous experiment presenting the following features: the presence of an epithelium in a connective-tissue medium with a reduced circulation; mucoid impregnation of the whole structure; the development of a granulation tissue and of areas of necrosis in the wall of the appendix. The regular fibrillary structure shows, further, that some of the changes are due to traction or pressure by the intra-abdominal viscera, to intestinal peristalsis, and to traction by omental adhesions.

The role of the epithelium in heterotopic ossification is known from experiments. The experimental transplantation of mucous tissues into connective-tissue media constantly results in hypertrophy and proliferation of the mucous epithelium. Sometimes the epithelium may be responsible for the secretion of a phosphatase (Lucinesco and Cavalli, 1935, 1936; Severi, 1939). Zones of necrosis are the usual sites of calcification. The histiocytes of the granulation tissue represent the source of the osteoblasts. Physiological studies have long ago shown that mucous substances and mechanical irritants have an osteogenetic effect. But even now there is no explanation of how haemopoietic tissue develops in relation to areas of heterotopic ossification.

Perusal of the literature revealed reports of calcification in appendicular mucoceles (Henke and Lubarsch, 1929; Olanescu *et al.*, 1942) and of three cases of actual ossification (Henke and Lubarsch, 1929). Two of the latter were published by Nishii and Akimoto (1928)—appendicular carcinomata associated with mucoceles, where osseous tissue appeared only in areas free of the invading neoplasm. The third was published from the Virchow-Krankenhaus (680/1928)—a case of partial appendicular mucocele containing in its walls osseous foci showing a regular fibrillary structure.

Summary

A case of heterotopic ossification of an appendicular mucocele is reported. Ossification was of wide extent and was associated with the appearance of haemopoietic tissue. The mucocele had perforated and was accompanied by a gelatinous condition of the peritoneum. The various conditions required for the onset of ossification—structural, biochemical, and mechanical—were present and are discussed. The condition was not suspected clinically, being discovered only at operation.

Bibliography

Carone, C. (1936). *Ann. ital. Chir.*, **15**, 461.
Cavalli, G. F. (1939). *Arch. ital. Med. sper.*, **4**, 321.
Cruickshank, M. M. (1936). *Indian med. Gaz.*, **71**, 28.
Frattin, G. (1937). *Arch. ital. Chir.*, **45**, 301.
Giuliani, G. M. (1934). Ibid., **38**, 645.
Guerrisi, A. (1938). *Folia med., Napoli*, **24**, 1196.
Henke, F., and Lubarsch, O. (1929). *Handbuch der speziellen path. Anat. u. Histol.*, vol. IV/III, p. 533. J. Springer, Berlin.
Huggins, C. B. (1931). *Arch. Surg., Chicago*, **22**, 377.
Jones, R. W., and Roberts, R. E. (1934). *Brit. J. Surg.*, **21**, 461.
Jung, A., and Cemil, S. (1935). *Presse méd.*, **43**, 140.
Kleine, H. O. (1929). *Arch. Gynäk.*, **139**, 145.
Koch, C., Schreiber, B., and Schreiber, G. (1939). *Ophthalmologica, Basel*, **97**, 284.
Leriche, R., and Lucinesco, E. (1935). *Presse méd.*, **43**, 137.
—— and Policard, A. (1926). *Les Problèmes de la Physiologie Normale et Pathologique de l'Os.* Masson, Paris.
Lucinesco, E., and Cavalli, G. (1935). *C. R. Soc. Biol.*, Paris, **120**, 139.
—— —— (1936). *Arch. ital. Chir.*, **42**, 581.
Merlini, R. (1931). *Arch. ital. Anat. Istol. pat.*, **2**, 1343.
Mönckeberg, J. G. (1902). *Virchows Arch.*, **167**, 191.
Neuhof, H. (1918–20). Studies from the Lab. of the Dep. of Surg., vol. III.
Nishii, R., and Akimoto, K. (1928). *Virchows Arch.*, **268**, 203.
Olanescu, G., Juvara, I., and Georgescu, C. (1942). *Rev. Chir., Bucuresti*, 622.
Paggi, B. (1936). *Policlinico, sez. chir.*, **43**, 328.
Regen, E. M., and Wilkins, W. E. (1934). *J. Lab. clin. Med.*, **20**, 250.
Reitmann, K. (1903). *Mschr. Ohrenheilk.*, **34**, 321.
Rollo, S. (1931). *Riv. Biol.*, **13**, 14.
Rosenstein, P. (1900). *Virchows Arch.*, **162**, 100.
Santa, L., and Marcacci, G. (1938). *Arch. ital. Chir.*, **49**, 593.
Scheidegger, S. (1939). *Schweiz. Z. Path. Bakt.*, **2**, 153.
Severi, R. (1939). *Boll. Soc. ital. Biol. sper.*, **14**, 456.
Törö, I. (1935). *Anat. Anz.*, **80**, 285.
Wurm, H. (1930). *Beitr. path. Anat.*, **85**, 401.

Medical Memoranda

An Unusual Case of Large-Bowel Obstruction

The following case of large-bowel obstruction after perineal excision of the rectum merits recording on account of its rarity. A search of the literature failed to reveal a similar case.

Case Report

A woman aged 54 was admitted to the wards of Mr. R. A. Keane at the North Staffordshire Royal Infirmary on Nov. 27, 1946, complaining of pain in the centre of the abdomen for three days. She had vomited on the morning of admission. A perineal excision of the rectum had been performed nine years previously and the colostomy had functioned adequately till one year ago, when a plastic operation was carried out for stenosis of the opening. Thereafter the colostomy had again functioned normally until two days before admission. There had been no bowel action since. There was also difficulty in micturition.

On examination the temperature was 98° F. (36.7° C.), pulse 88. The tongue was furred. The abdomen was soft, and a large median swelling was visible in the suprapubic region which was tender and resonant on percussion. Normal bowel sounds were heard and there was no evidence of intestinal colic during examination. A left inguinal colostomy was present which looked quite normal, but it was impossible to introduce a finger into either opening.

Operation. Under general anaesthesia—nitrous oxide, oxygen, "trilene," and ether—a right paramedian subumbilical incision was made. A gangrenous mass of large bowel presented in the wound. This proved to be the blind efferent loop of large bowel leading from the colostomy. It was not fixed distally to the pelvic floor, but hung free in the peritoneal cavity as a pendulous sac. This sac was about 8 by 3 in. (20 by 7.5 cm.) in size, had undergone torsion at its base, and was bluish in colour. This blind end of colon was resected, leaving about a 1½-in. (3.75-cm.) stump at the colostomy. Free blood-stained fluid was mopped out of the pelvis, revealing the uterus firmly attached to the sacrum by adhesions on its whole posterior surface. Sulphathiazole, 5 g., was inserted in the peritoneal cavity and the abdomen was closed with a stab drain to the pelvis. The colostomy acted profusely before the patient left the table. Examination of the specimen showed a black gangrenous mucosa; the sac of bowel contained a heavy, putty-like faecal mass about the size of an orange and with a most offensive odour. Convalescence was uneventful, and the patient was discharged home on the sixteenth day.

Comment

This unusual complication of perineal excision of the rectum could occur only where the distal segment of bowel was hanging free and was not fixed in the usual manner to the reconstituted pelvic floor. This and the adherence of the uterus to the sacrum suggest either that an inadequate repair of the pelvic peritoneum had been carried out or that it had broken down post-operatively. The weighty faecal mass was presumably a precipitating factor.

My thanks are due to Mr. R. A. Keane for permission to publish this case.

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Reviews

DOCTOR POL

Nicolaus Pol Doctor 1494. By Max H. Fisch. With a Critical Text of his Guaiac Tract edited with a translation by Dorothy M. Schullian. (Pp. 244; illustrated. $7.50.) New York: Published for the Cleveland Medical Library Association by Herbert Reichner, N.Y. 21.

The contents of a medical library of early date may furnish an interesting commentary upon the contemporary state of medical knowledge. Consequently, a library which was built up during the early years of the sixteenth century is of surprising interest, and as each item in the collection to which this book refers is marked by the signature "Nicolaus Pol Doctor 1494" there is no difficulty in identifying the volumes when they are found. The date, as we shall presently show, does not refer to the book on which it is inscribed. The books and manuscripts of Nicolaus Pol originally numbered some 1,300 items, and those which still exist are now widely scattered. The present account is based upon the Cleveland Collection, which has had the following curious history.

In 1907 a young antiquarian bookseller in Munich, Maurice Ettinghausen, sold to Dr. E. C. Streeter, of Boston, a bundle of some thirty incunabula and sixteenth-century books, each bearing the inscription of Nicolaus Pol. Twenty years later, as head of Maggs Brothers, he visited Boston and bought back the collection. Catalogued and placed on sale, it was acquired for Cleveland Medical Library through the services of Harvey Cushing and his nephew Edward H. Cushing, and once more it crossed the Atlantic. In America it remains as one of the richest treasures of the Cleveland Library. There were already 13 of Pol's books in the Yale collection, and a search in various libraries of Europe revealed many more. At San Candido, in Tyrol, 133 volumes were found. Others came to light at Innsbruck University, and a few elsewhere, although many are still untraced.

In the meantime Dr. Max H. Fisch has rendered useful service by publishing a catalogue of Nicolaus Pol's library so far as it is known. The work is, however, much more than a mere catalogue of this fine medical library of Renaissance date. From the scanty data available he has been able to construct a brief biography of the man himself. The place and date of his birth are uncertain; Tyrol, about 1470, is a rough guess. But we do know that in 1487 he was appointed Court Pharmacist to Duke Sigismund at Innsbruck at the beggarly salary of twenty florins a year, and in 1495 he became physician to the Emperor Maximilian at a hundred florins a year. The document ratifying this appointment is preserved at Innsbruck and is reproduced as Plate I in this work. The date 1494, appended to each of his signatures in his books, may possibly have been the year in which he started medical practice. Certainly he was in no position to buy many books then. Between 1513 and 1520 his doings are revealed in a number of letters between Pol and Veit Bild, a monk of Augsburg, who appears to have acted as Pol's agent in purchasing books. A number of books are mentioned in the letters, including those of the Spanish astrologer Ramon Lull. Twenty works by Lull are included in the present list. It seems probable that Pol was a member of the commission sent to Spain by Cardinal Lang in 1517 to study the guaiac treatment of syphilis, and from this mission there emerged his tract *De Morbo Gallico*, written in 1519 and now reproduced in full in Latin and English (pp. 50–97). The excellent translation is the work of Dorothy M. Schullian. The decoction of guaiacum wood, taken with a much reduced diet, was doubtless a valuable alternative to mercury, which killed as many as it cured. No doubt Pol passed from the service of Maximilian to that of Charles V; certainly he continued to reside at Innsbruck, and there he died in 1532.

The second half of the book contains a list of the known works of this interesting library and of their present location. Among the titles one notices Aesop's *Fables*, 14 works of Albertus Magnus, Arnold of Villanova's *Regimen of Salerno*, Avicenna's *Canon of Medicine*, Bartholomaeus Anglicus's *De Proprietatibus Rerum*, Bernard de Gordon's *De Urinis and De Pulsibus*, John of Gaddesden's *Rosa Anglica*, Guy de Chauliac's *Chirurgia*, Sir Thomas More's *Utopia*—one is tempted to continue, for the very names have a fascination, but the variety is already obvious. It is a catalogue most attractive to the bibliophile. Four of the lovely bindings are reproduced as plates, and there are excellent portraits of Maximilian, Cardinal Lang, and Jacob Fugger. Other plates depict the guaiacum plant and its preparation as explained in Pol's book, as also in the more famous tract of Ulrich von Hutten. Unfortunately there is no portrait of Nicolaus Pol, who, to judge from his library, must have been one of the leading medical scholars of his time. This beautiful book reflects high credit on author and publisher alike.

DOUGLAS GUTHRIE.

GUIDE FOR STUDENTS

Symptoms and Signs in Clinical Medicine. An Introduction to Medical Diagnosis. By E. Noble Chamberlain, M.D., M.Sc., F.R.C.P. Fourth edition. (Pp. 464; 346 figures, of which 19 are in colour. 30s.) Bristol: John Wright and Sons. 1947.

The bewilderment of the first few weeks in the medical wards is an emotion so intense that most medical men can recall it for years afterwards. It may be that the introductory courses now ordained by the General Medical Council prepare the clerk for his ordeal, but the need for some elementary written guide remains. Dr. Noble Chamberlain's book is designed to meet this need, and a measure of his success is given by its having passed through four editions and five reprintings in less than twelve years. Such popularity suggests that the book provides the student with what he believes he needs and forestalls criticism.

There are difficulties in reviewing a book addressed to a group of which the reviewer is not a member, for all teachers must hold their own views on what the student starting medicine should be taught. These views may differ not only from those of other teachers, but also from those of the student himself. Dr. Chamberlain's approach is conventional and unexceptionable, but the danger of this method is of reducing the patient to a disarticulated collection of systems and organs. Many would consider to be inadequate his definition of diagnosis as implying "knowledge of the organs or tissues affected by disease, and of the pathological changes which have taken place in them." His introductory chapter might with advantage stress the importance of the patient as an individual and a biological unit in the social structure. These are aspects which the student appreciates only when he is plunged into practice and finds himself no longer surrounded by "cases of mitral stenosis" but by sick people. The descriptions of methods of examination and of physical signs are excellent, and most of the half-tone illustrations apposite and well produced; some of the colour plates are less successful. This edition will continue to guide the student satisfactorily through the maze of his first period in the medical wards.

R. BODLEY SCOTT.

NURSING OF CHILDREN

Textbook on the Nursing and Diseases of Sick Children for Nurses. By various authors. Edited by Alan Moncrieff, M.D., F.R.C.P. Fouth edition. (Pp. 744; 154 illustrations. 30s.) London: H. K. Lewis and Co. 1947.

The new edition of this excellent book on the nursing and care of sick children is larger by 100 pages and has a number of new illustrations; one or two contributors have been changed, and it has been thoroughly revised; but it is substantially the same book, and bears on every chapter the authoritative stamp of Great Ormond Street. Although the book is well known and established, it deserves something more than a brief notice and commendation. Its purpose is to serve as a manual for student nurses training in children's hospitals and to prepare them for the examinations necessary for entry on the State Register of Children's Nurses. Its excellence is partly, perhaps largely, due to the happy combination of the medical, surgical, and nursing staff of Great Ormond Street Hospital in planning and writing it. In the preface we come across the phrase "scientific

nursing." The book is more than an account of that, for its teaching is scientific, practical, and "humane."

The first chapter is on the "humanity" of children's nursing; it is an inspiring guide to the young nurse entering on her new work, describing the essential qualities needed by the nurse of sick children, and a general picture of her work and of the high obligations that rest upon her. As a compendium of principles, standards, and tradition, and as an introduction to the whole subject, this short opening chapter could hardly be bettered. The succeeding chapters are on the practical and scientific aspects of nursing in general, and the authors give simple and clear directions on nursing techniques accompanied by concise scientific explanations. The authors of the second part of the book discuss, chapter by chapter, the diseases of children, as well as the subject of dietetics. They preserve throughout a successful blend of the practical and the scientific, with the proper emphasis on nursing. The book closes with a number of short but useful appendices.

The editor, Prof. Alan Moncrieff, and his medical and nursing collaborators are indeed to be congratulated on the past success and present merits of this book. They have done good service in promoting and spreading through Great Britain the high standard of nursing long associated with the Great Ormond Street Hospital. It would perhaps be risky for the reviewer to suggest any improvement in a book so successful and so carefully planned and replanned. But the young nurse, a little bewildered by the multitude of diseases with their many names and symptoms, might be helped by a short section giving a general and simple account of pathology and of the special pathological features of children's diseases.

CHARLES MCNEIL.

ELECTRONICS

Electronics and Their Application in Industry and Research. Edited by Bernard Lovell. (Pp. 660; 404 figures. 42s.) London: The Pilot Press. 1947.

If electronics as a science may be said logically to have begun with the discovery of the electron by Sir Joseph Thomson, the second world war was the primary influence, as Dr. Lovell points out, "which changed electronics from a science auxiliary to physics and electrical engineering to a subject with an independent organization." This book might be described as an account of its frontiers by a team of specialists. These include Dr. L. G. Grimmett, formerly senior physicist to the radiotherapeutic research unit of the Medical Research Council, who writes on electronics in medicine, and Dr. R. J. Pumphrey, of the Cambridge Department of Zoology, who surveys its physiological uses. What follows refers mainly to these two sections, but they are typical of the volume as a whole.

Dr. Grimmett begins with an account of available methods for the acceleration of charged particles to very high energies, emphasizing chiefly the generation of high-voltage *x* rays from electron beams of equivalent energy and the still experimental technique of neutron irradiation. Progress in the development of dosimeters is also recorded, and there is a highly compressed account of the tracer method. We may criticize the latter for the lack of warning that radioactive trace elements should be used in minimum amounts needed to ensure both safety and validity of results. Other matters discussed include the bacteriological uses of the electron microscope, the recording of bio-electric potentials, and acoustical applications. For Dr. Pumphrey the recording of bio-electric potentials becomes a main rather than a subsidiary subject. In contrast with Dr. Grimmett, who writes as a physicist, he gives a historical and critical survey of the electrical aspect of nerve-impulse transmission, leading up to a brief discussion of present uncertainty about the synapse mechanism. It may seem ungrateful to suggest that from the material which is compressed into these two chapters alone at least three books could usefully be written—on radiotherapeutics, the tracer technique, and electronics in biological research. Meantime, although their combined length is no more than 60 pages, they bring together much information which is not readily available and are accompanied by useful bibliographies. Other chapters which should be of interest to the medical research worker are on electron physics, photocells, and the electron microscope.

A. W. HASLETT.

BOOKS RECEIVED

[Review is not precluded by notice here of books recently received]

L'Année Thérapeutique. By A. Ravina. (Pp. 185. 220 francs.) 18th ed. Paris: Masson. 1946.

A short account of new therapeutic measures.

Les Syndromes Douloureux de la Région Épigastrique. Vols. I and II. 4th ed. By R. A. Gutmann. (Pp. 739 and 766. No price.) Paris: Gaston Doin. 1947.

A general account of the conditions causing upper abdominal pain and their treatment.

L'Aphasie et la Désintégration Fonctionnelle du Langage. By Th. Alajouanine and P. Mozziconacci. (Pp. 156. 450 francs.) L'Expansion Scientifique Française. 1948.

A monograph on the clinical aspects.

Les Maladies des Végétaux. By J. Magrou. (Pp. 374. 800 francs.) L'Expansion Scientifique Française. Paris: 1948.

A textbook of plant diseases.

No Retreat from Reason. By A. E. Cohn. (Pp. 279. $3.50.) New York: Harcourt, Brace. 1948.

Essays on medical history, research, and practice.

Taylor's Principles and Practice of Medical Jurisprudence. Vol. I. Edited by S. Smith, C.B.E., M.D., F.R.C.P.Ed., D.P.H. 10th ed. (Pp. 723. 45s.) London: J. and A. Churchill. 1948.

New material is incorporated in this well-known textbook.

Diseases of the Eye. By Sir John H. Parsons, C.B.E., D.Sc., F.R.C.S., F.R.S., and Sir Stewart Duke-Elder, K.C.V.O., M.D., F.R.C.S. 11th ed. (Pp. 732. 30s.) London: J. and A. Churchill. 1948.

This edition incorporates recent advances, particularly in the use of sulphonamides and antibiotics.

A Rorschach Study on the Psychological Characteristics of Alcoholics. By C. Buhler, Ph.D., and D. W. Lefever, Ph.D. (Pp. 64. $0.75.) Connecticut: Hillhouse Press. 1948.

A monograph on the study of 60 patients.

Modern Audiometric Technique. Part 1. By B. M. Green. (Pp. 48. 5s.) Melbourne: Modern Hearing Aids. 1948.

A concise account for audiometrists.

Introduction to Psychiatry. By W. E. Biddle, M.D., and M. van Sickel, B.S., R.N. 2nd ed. (Pp. 344. 14s.) Philadelphia and London: W. B. Saunders. 1948.

An introductory textbook for medical students and nurses.

Alsos. The Failure in German Science. By S. A. Goudsmit. (Pp. 259. 15s.) London: S.I.G.M.A. 1947.

An account of the Germans' investigations into the production of atomic weapons.

The Sick African. By M. Gelfand, M.B., Ch.B., M.R.C.P., D.M.R. 2nd ed. (Pp. 699. 38s.) Capetown: Stewart Printing Company. 1948.

A clinical account of recent methods of diagnosis and treatment of diseases common in Africa.

The Rh Factor. Edited by J. M. Hill, M.D., and W. Dameshek, M.D. (Pp. 192. No price.) New York: Grune and Stratton. 1948.

A collection of papers forming a special issue of *Blood*.

Handbook and Atlas of the Slit-Lamp Microscopy of the Living Eye. By A. Vogt. (Pp. 1,058. £16 10s.) Zurich: Schweizer Druck und Verlagshaus. 1948.

The author gives an account of the iris, vitreous body, and conjunctiva, and includes a discussion of the inheritance of senile cataract.

Epitome of the Pharmacopeia and National Formulary. 8th ed. Edited by A. Smith. (Pp. 238. 15s.) London: J. B. Lippincott. 1947.

Issued by the Council on Pharmacy and Chemistry of the American Medical Association.

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WHAT WE HAVE GAINED

The statement by the Council drawn up at the end of its long meeting on May 5 after consideration of the results of the plebiscite was printed on a loose sheet which was inserted into last week's *Journal*. As the number of general practitioners voting No in answer to Question B fell far short of the 13,000 required if collective opposition to the Act was to be continued, the Council is recommending the Representative Body to be prepared "to co-operate in the new service on the understanding that the Minister will continue negotiations on outstanding matters, including terms and conditions of service for consultants and specialists, general practitioners, public health officers, and others." The Council also resolved to accept the Minister of Health's invitation to enter immediately into discussions on the details of the promised Amending Bill, and on other outstanding matters. The Council's decision has been widely hailed by the Press as wise and statesmanlike. That this decision was right finds support in our correspondence columns from that Nestor of medical politics, Dr. Alfred Cox, who was Medical Secretary of the B.M.A. in 1911 and retired after long years of service in 1932. His views, we believe, will carry great weight with the representatives who are to attend the Special Meeting on May 28. "Our best policy," Dr. Cox believes, "is to accept the verdict of the plebiscite ungrudgingly and to assure those doctors who join the Service that they will have the whole-hearted support of the Association in making the Service a credit to the profession." He recalls the familiar observation made by the *Westminster Gazette* in 1912 and refers to the comment made in the *Economist* about a fortnight ago: "Undoubtedly the doctors have won a big victory, for Mr. Bevan does not easily climb down to the extent that he has done."

Some correspondents have taken this *Journal* to task because of the content and tone of the leading articles that have appeared since Mr. Bevan's statement in the House of Commons on April 7. We avoided using the words of the *Economist* because it seemed ungracious to crow over Mr. Bevan when he made a generous gesture in unexceptionable terms. But our critics seem not to have realized how far the situation has changed since December of last year, and, indeed, since the time when Mr. Ernest Brown, Liberal National Minister of Health in the Coalition Government, put forward his proposals for a health service in 1943. We may recall that the Coalition Government then proposed that general practice should be carried on in health centres manned by whole-time full-salaried doctors with no right to private practice. The young medical man would enter this service at a salary of £400 a year, and by the time he was 46 would not ordinarily be earning more than £1,200 a year. We have only to contrast the scheme put forward by a Liberal Minister of Health with the present scheme to see what great changes have been made as a result of the intermittent negotiations that have been going on for the past five years. The Central Medical Board in Mr. Brown's and in Mr. Willink's scheme had wide powers over the general practitioner, including the power of appointment. The first move away from this situation was to devolve on Local Executive Councils with full professional representation the principal responsibility for selecting men for vacancies in general practice. Mr. Bevan has now finally devolved this responsibility where it should properly lie—the general practitioner himself, who has the right to choose his partners and assistants. Mr. Bevan, too, has accepted the Spens Committee recommendations on remuneration for general practitioners, which go far beyond the mean proposals of Mr. Ernest Brown.

When Mr. Ernest Brown and Mr. Willink were Ministers of Health the B.M.A. strongly opposed the idea that the new health service should be administered by local authorities. There was particular objection to the municipal control of hospitals, and as an alternative it was advocated that they should be administered in regions based on universities. The opposition was so effective that the municipalization of the hospital service was abandoned and the regional idea was accepted. Mr. Brown would have allowed in his scheme no private practice to the general practitioner. The B.M.A. successfully resisted this, and Mr. Bevan in his Act has granted the right to private practice to general practitioners and to consultants and specialists. Free choice of doctor being incompatible with a full-salaried service, the B.M.A. won its point that payment should be principally by capitation fee, and Mr. Bevan now has removed the objectionable feature of the universal basic salary, which many people with reason saw as an attempt to control certification. When the Negotiating Committee met Mr. Bevan in December of last year it presented a fully argued case on the ambiguities of Sections 35 and 36 of the Act. Mr. Bevan then took no notice of these objections, but has since set up a legal committee to inquire into them with the promise of amendment in the terms of the legal committee's findings. Another point pressed upon Mr. Bevan was that health centres should be the subject of experiment. Mr. Bevan, though pressed on by the Socialist Medical Association and its supporters, has refused to be hurried in the matter of health centres. In the first place, building materials and labour will be more usefully employed in providing new houses, and in the second place he has agreed with the B.M.A. view that further inquiry is needed. Mr. Bevan has met the professional demand for free expression of opinion on all aspects of the Service, and will put in the contract an assurance that this will be safeguarded. He has, too, promised to submit Regulations in draft to the B.M.A. Although he retains his power of negative direction, he has restricted this by agreeing that any doctor should practise where he likes in those areas not defined as being over-doctored. In fact, when we review the situation as it has evolved since the first plans of the Coalition Government were made known, it

is clear that the medical profession has by its tenacity in negotiation made very considerable gains. There was a fear in the early months after the publication of the Beveridge Report that the Government would introduce only the medical part of its social security plan, and the B.M.A. stated[1] that it would co-operate with the Governmen if Parliament "decided to accept the assumptions of the Report and to put into operation the proposals of the Report, taken as a whole. . . ." The conditions of co-operation have been fulfilled.

The medical profession has not succeeded in persuading Mr. Bevan to grant the right of appeal against the decision of a tribunal of the Minister to remove a man from the Service. It has failed to persuade the Minister to remove his power of negative direction, and it has failed to remove from the Act the prohibition against buying and selling public practices. This last point is one of much importance to general practitioners. But Dr. Cox has put the matter in a nutshell when he writes: "To continue to oppose the working of the Service because we have failed on the goodwill issue would be to fly in the face of what is possible." In addition to the reasons he gives to support this statement there is the fourth and compelling reason of the economic position of the young man entering general practice to-day. The ownership of goodwill was a defence against a full-salaried service and also gave to the owner the right to choose his partner or assistant. Mr. Bevan, by his own decision, has made the introduction of a full-salaried service under the present Act impossible, and he has restored to the general practitioner the right to choose his own partner and assistant.

It would seem that some of our correspondents do not have a "whole-hearted desire," or, indeed, any desire at all, for a comprehensive medical service available to the whole community. This is a tenable position, but it is not the policy of the British Medical Association. The Representative Body has accepted a service available to 100% of the community. Valid arguments can be brought against the inclusion of the whole population in a National Health Service, but again the exclusion from such a service of 10% or 15% of the population is not B.M.A. policy. We recall the observations made by Dr. H. Guy Dain, the Chairman of Council, at the Special Representative Meeting two years ago.[2] As reported, he said "that in his view the question of proceeding to get anything less than 100% was dead. Their opponents would be delighted to see them come out and claim that the Service should be for less than 100%. He would not say that he was in favour of 100%, but he had never seen any method of dividing the population for a complete medical service, though it might be done with the present restricted N.H.I. service." Through its representative organization the medical profession has since the publication of the Beveridge Report reiterated its desire for the comprehensive medical service available to the whole community that was the fulfilment of Beveridge's Assumption B. A succession of Ministers of Health have yielded ground in the face of the B.M.A.'s sustained opposition to certain of their proposals. Mr. Bevan, in the light of his own statements and of the policy of his own Party, has by his promise of an Amending Bill and other concessions in written answers to questions gone a considerable way to meeting the demands of the medical profession. He has offered a compromise, and compromises are the traditional English way of settling disputes. For the medical profession to reject the compromise and to be intransigent would cost it the support of public opinion. The B.M.A. Council, viewing the situation as a whole, has made what is widely acclaimed as a wise decision in recommending the Representative Body to co-operate with the Government in launching the new service. Much remains to be done, and the profession's negotiators will need its support and trust in moulding the new service through the vigilant oversight of Regulations and in securing satisfactory terms and conditions. During the past months the medical profession has shown its strength and has shown, too, that it can use it with wisdom.

[1] *British Medical Journal*, 1943, **1**, 193.
[2] *British Medical Journal Supplement*, 1946, **1**, 133.

WAR AND MEDICAL RESEARCH

The Medical Research Council has performed a useful service in bringing together in the shape of a Command Paper an account of the manifold work which was done under its auspices during the war. Those who live during a period of great events seldom appreciate the magnitude of such events until later when the opportunity arises to see them in retrospect. Every month or every week during the years of the war seemed to bring to the fore some outstanding piece of medical investigation in one or other field, but it is only when these investigations are described in a connected narrative that we are able to realize how numerous they were, what an enormous field of inquiry they covered, what an army of experts was enlisted, and how decisive many of the results were in the conquest of disease, in the protection of those exposed to unusual hazard, and in the rehabilitation of those who had suffered wounding or other injury.

The pace of medical science is accelerated in wartime. The slow-growing plant of medical research undergoes a forcing process. This is due in large measure to national urgencies, requiring instant solutions of problems which otherwise would have been attacked more leisurely. But there is another reason why medicine, both medical research and medical service in general, makes advances during war. War is a challenge to medicine. Medicine is concerned with the saving of the individual life and the reduction of suffering. With the outbreak of war the nations concerned are delivered over to destructive forces with which the single life counts as nothing at all. The impulse to go forward with medical work of any kind is due in part to the desire to fortify threatened ideals and to save something for sanity in a mad world. Yet by a strange irony medicine itself contributes enormously to the very effectiveness of the war machine. It enables men to sustain the struggle as they never would if the resources of medicine were not available, and even when they fall wounded it restores and re-equips them so that often they can go into the fighting line again. In the campaign in North-Western Europe in 1944–5 it was estimated that if the British soldier wounded in the field of battle came into

the hands of the medical service the chance of his survival was about 93%, and of his recovery to a degree fitting him for a reasonably wide range of employment 84%. Until the final stage of atomic bomb devastation it could be said that advances in methods of destruction had been matched by advances in saving life. Thus medicine may be said to prolong and intensify the combat. It can even force military decisions. The effective introduction of malaria suppression by mepacrine was decisive in the overthrow of Japan, as it permitted military operations to be conducted successfully whereas otherwise they would have been impossible.

Much of the work described in the Medical Research Council report, reviewed on other pages, will be familiar to our readers owing to the fact that during the war years there was constant publication. Only a very partial censorship descended upon medical achievements. This is shown by the fact that there are not far short of two hundred references to wartime papers published in the *British Medical Journal* alone.

The report surveys the work done on the treatment of wounds and injuries and of war diseases, the work on nutrition, the investigations which come under the term "personnel research," the emergency services, such as those concerned with immunological supplies and with blood transfusion, the preparation and maintenance of biological standards, and much more. A great deal of the work done, such as the organization of a public health laboratory service, remains as a legacy bequeathed by war to peace. One golden thread runs through all the narratives. Those engaged in medical research of one sort or another not only gave their outstanding abilities and often uncommon genius to the national effort but served with a personal devotion, a courage, and a sacrifice in their laboratories or wherever it might be, worthy of the similar qualities shown by the men in the fighting Forces. Those concerned at the National Institute for Medical Research, for example, were studying the physiological effects of high oxygen tension, which meant entering a pressure chamber; 300 such "dives" were taken with a fine disregard of personal distress. At the same centre the problem of protection against flame was being studied and tests on certain skin pastes called for a high degree of personal courage. So with the experiments on "climatic physiology" carried out in "hot rooms" at the Admiralty, involving a tremendous strain on those concerned, with frequent heat collapse and cramps. Soon after the outbreak of the war, when it was evident that rationing on a scale to which the British people had never been accustomed would have to be enforced, the two members of the staff of the Department of Experimental Medicine at Cambridge intimated that they and certain attached workers were prepared, in advance of compulsory rationing, to subsist voluntarily for a period of weeks or months on a very restricted dietary scale, suddenly imposed, in order to observe its physiological and psychological effects on the health of adults of both sexes. Their rations were planned to correspond exactly with those which might be expected to be available for the general population under very severe blockade conditions. Actually the diet which these workers accepted was more restricted than was afterwards proved to be necessary, but their experiment materially influenced subsequent policy concerning food rationing. Another example was afforded by the twenty volunteers—conscientious objectors to military service—who served as subjects for experimental transmission of scabies and who later collaborated in important dietetic experiments, subsisting on a diet as deficient as possible in vitamin A and carotene. There were also volunteers who underwent experimental infection with jaundice in pursuit of the investigation of infective hepatitis. Some of these were rheumatoid arthritis patients who hoped that an attack of jaundice might relieve their condition—as it did temporarily—but others were inspired by the pure zeal of the investigator.

The report includes an extended tribute to three distinguished men in medical research, two of whom died during the war (Sir Patrick Laidlaw and Sir Thomas Lewis) and the third (Sir Henry Dale, O.M.) retired from the service of the Council after being a member of the staff for twenty-eight years. It is considered worthy of note at a time when the question of attracting the best brains to scientific work in the Government service is being much debated and reported upon that three such men as Laidlaw, Lewis, and Dale, of the highest international fame in medical research, should have given their best years, with an average period of a quarter of a century, to the service of the Medical Research Council.

THE MYSTERY OF THE EOSINOPHIL

An increase in circulating eosinophils is a feature of a number of disorders which otherwise appear to have little in common. There are groups of conditions, such as allergic diseases of all kinds, parasitic infestations, and cutaneous eruptions, in which we can at least say that sensitization, a metazoan parasite, or a visible skin disease links the group together. But outside these categories come a number of other conditions which appear to have nothing to do with the three main groups. One of these is lymphadenoma: enlargement of lymph glands with eosinophilia nearly always leads to the diagnosis of that disease. The eosinophilia may be very marked indeed and extend to 50% or more of the total leucocytes, themselves abnormally increased. Some have felt that this implies an allergic background, and attempts, apparently unsuccessful, have been made to prove sensitization by intradermal inoculation of lymphadenomatous material. It is probable that in this disease the eosinophilia in the blood is the result of an overflow from the eosinophil deposits in the affected lymph glands, and that it is therefore analogous to the lymphocytosis in lymphatic leukaemia. Eosinophilic leukaemia may be considered as a disorder linking the true leukaemias and lymphadenoma, and lymphadenoma should be looked upon as one of many possible forms of malignancy in an organ with many functions and an eventful embryonic career.

Sometimes, however, eosinophilia with enlargement of lymph glands occurs in serum sickness and may be confusing. The presence of heterophilic antibodies to sheep red cells differentiates the two conditions—the test for these is so unpredictable and apparently irrational that it recalls some of the methods of mediaeval medicine in its more esoteric phases.

Allergic eosinophilia is most variable in its appearance. Many patients with severe asthma have no eosinophilia; on the other hand, there may be marked eosinophilia in patients who react acutely for the first time to certain drugs or foodstuffs.

Symptomless eosinophilia is most often due to metazoan parasites, and in certain parts of the world where helminth infestation is universal eosinophilia is equally common. In the tropical belt of Africa infestation by *Filaria perstans* is both symptomless and practically universal, at least in some areas, and the eosinophils may amount to 70% or more of the circulating leucocytes. It should be remembered that amoebiasis does not cause eosinophilia—protozoa never evoke a response which is essentially metazoan. For some time to come helminth infestation must continue to be carefully excluded in adult males with eosinophilia, particularly in those who, interned in Japanese prison camps, so commonly contracted hookworm and *Strongyloides* infestation.

A further condition commonly associated with eosinophilia is periarteritis nodosa. This disease is to-day recognized to be more common than was once believed, and a proportion of the cases recover. Unless a biopsy is possible on a skin nodule the diagnosis of the condition must always be a guess; but eosinophilia is commonly encountered, and where albuminuria, fever, and eosinophilia are found together this disease must at least be considered. The contemporary view is that the condition is allergic, and the eosinophilia certainly gives this some support.

Of recent years there have been separated certain other conditions, all rare, in which eosinophilia is present in tissues or circulating blood and where some authorities have thought it possible to define clinical entities. One such condition is eosinophilic granuloma of skin, detailed studies of which have recently been published.[1] Clinically the disease is stated to be a chronic and usually self-limited condition in which doughy, firm, reddish-brown tumours form in the skin. The diagnosis is essentially a laboratory one, since eosinophilia of the order of 50% is present in the circulating blood and also in the actual lesions. The condition is strikingly similar histologically to periarteritis nodosa, since the lesions occur in relation to small blood vessels and perivascular tissue. Allergy has also been confirmed in some cases; for example, a *Trichophyton* was grown from the feet of a patient, and trichophytin extracts gave positive intradermal reactions.

A much-disputed eosinophilic disorder of the lungs was described by Löffler[2] in 1932, and a similar condition, commonest apparently in India, is known as "tropical" eosinophilia. A survey of the latter condition has recently been made by Joseph,[3] who considers the two disorders distinct. But in certain cases such as that described by Perlingiero and György[4] infestation with roundworms has been present. Indeed, so many types of worms pass through the lungs at one stage of their life cycle that pulmonary symptoms due to their presence are inevitable. Very definite proof that a parasitic infestation is absent must be demanded before accepting these disorders as new entities. The discovery of mites in the sputum of patients must be accepted with abundant reserve. Entomologists tell us that their peace of mind is constantly being undermined by reports of mites in sputum, urine, or faeces. The truth is that mites are everywhere and easily fall into containers later filled with pathological material.

Eosinophilic granuloma of bone is a much more distinct entity. It was first described by Finzi[5] in 1929, and something under fifty cases have been recorded. It is now generally agreed that the condition is one stage in the development of a disturbance of lipoid metabolism, and that the cumbersomely named Hand-Schüller-Christian disease is essentially the same disorder at an earlier stage. Other conditions in which tissue or blood eosinophilia may be present are numerous, but in most of them the eosinophilia is erratic and of most uncertain significance. In the whole gastro-intestinal tract, for example, acute inflammation is often eosinophilic; in widespread secondary malignant deposits blood eosinophilia has been recorded, but is not the rule; eosinophilia in blood and tissues occurs in some cases of radium sickness; and on occasion eosinophilic pleural effusions are found which appear to have no common aetiology or prognostic significance.

There is, in fact, no apparent link between all the varied conditions in which eosinophils are a prominent feature. But it is worth remembering that ignorance about the function of all other leucocytes, except the polymorph, is as great. No one has suggested what function a basophil cell or a monocyte may be expected to carry out. Lymphocytes amount to 40% of circulating cells, yet few haematologists would like to be dogmatic about their purpose. If the eosinophil is a mystery, it is at least in good company.

[1] Weidman, F. D., *Arch. Derm. Syph., Chicago*, 1947, **55**, 155; Lewis, G. M., and Cormia, F. E., ibid., 1947, **55**, 176; Lever, W. F., ibid., 1947, **55**, 194; Dobes, W. L., and Weidman, F. D., ibid., 1947, **55**, 212.
[2] Löffler, W., *Beitr. klin. Tuberk.*, 1932, **79**, 368.
[3] Joseph, A. D., *Indian med. Gaz.*, 1946, **81**, 515.
[4] Perlingiero, J. G., and György, P., *Amer. J. Dis. Child.*, 1947, **73**, 34.
[5] Finzi, O., *Minerva med., Torino*, 1929, **9**, 239.

POLICY FOR PEOPLES

The relatively high birth rate in this country in 1946 and 1947 has silenced temporarily the talk of a persistent and cumulative decline in population. Not long ago the view was put forward that the population of Great Britain might well be declining by a quarter or more in each generation before the next half-century was out. It was even predicted that by 1948 there would be some fall in total numbers; this has not occurred, and a large decline seems now more remote. Predictions in this field, of course, cannot be much better than guesses. This is borne out by a table which appears in a report on *Population Policy in Great Britain* just published by P E P (Political and Economic Planning).[1] Five different assumptions are made regarding mortality and fertility trends in England and Wales during the next hundred years. If we take the most pessimistic of them it leaves us with a population at the end of that time of something like 14 millions, and if we take the most optimistic we have a population in the 'forties of the next century of 43 millions, which is very much what it is at present. According to the results of some research at Princeton University the population of the British Isles may have fallen by 1970 from something over 50 millions to under 47, while that of Soviet Russia (its pre-war territories

[1] *Population Policy in Great Britain.* A Report by P E P. (P E P., 16, Queen Anne's Gate, S.W.1. 15s. net.)

only) will have risen from 174 to 222. These are interesting exercises in what the statisticians call "projection," but the unknown factors are so many that the results must be subject to heavy discounts.

During the recent war there was a relatively high level of fertility in this country. The "baby slump" of the 1914–18 war was not repeated. In the Netherlands during the year after liberation the birth rate was higher than ever before in their history; in France it was the highest for a quarter of a century, and it rose even in Germany. Evidently if there is a "retreat from parenthood" it is not an orderly and continuous retreat; there are hesitations and retracings. Nevertheless, the practice of family limitation has spread gradually from groups of the highest social standing to all classes of the population in this country and in a large part of western Europe. With wider opportunities for advice on birth control a fall in the birth rate is only to be expected, though with relatively fewer people dying a decline in population can be temporarily avoided. For a time birth control and death control may keep in step. But the childless marriage and the one-child marriage will be more frequent; there will be fewer unwanted children and fewer intentional abortions; and if it should come about that all parenthood is voluntary so much the better both for parents and offspring, but without some policy at national level the numbers of the population may fall catastrophically.

The term "population policy" would have scandalized our forebears, who took bitter exception even to Malthus's well-intentioned proposals for postponed marriage, not to speak of the neo-Malthusian advocacy of control of fertility by contraception. There are individualists who maintain that no attempt should be made to influence people's reproductive behaviour. Authoritarian banning of non-injurious contraceptives is now out of the question, and mere exhortation to people to have more children is futile. A population "drive" would cover itself with ridicule. Parliament cannot deal with the unborn generations as it deals with the gas industry or with doctors. But a population policy directed to the encouragement of parenthood can be pursued in ways which are very ably set forth in this P E P report. One measure is obviously financial assistance to parents by means of maternity grants, family allowances—the present family allowances, in the opinion of P E P, should be doubled—social insurance, and tax rebates. These of course should be accompanied by the provision of suitable houses and other environmental health services. A case might also be made out for low-interest marriage loans. These measures for the encouragement of parenthood, which are already in being to a greater or less extent, can be advocated on grounds of social justice apart altogether from prospective population; but, as someone has remarked before, if children are not had for love they are not likely to be had for money. Over and above all inducements is something imponderable—the raising of the status of family life. A large family was once the subject of pride; later it became a subject of jest, and even of reproach on the ground of imprudence. There are signs, however, that the bringing up of children is enjoying a new prestige. The Rev. Mr. Quiverful is now a more highly esteemed citizen of Barchester.

The principal proposal in the P E P report hinges on the National Health Service, from which P E P expects a great deal. The Service, it says, provides the setting for a revolutionary advance in personal health care of the individual and family. It even gives the Minister of Health the additional portfolio of Minister of Population. Within the National Health Service it desires to see a Family Welfare Service in which the general practitioner, fortified perhaps by a code of practice prepared by the British Medical Association, will be the pre-marital adviser. Well, we pause there. It is admitted at once, of course, that the health of the parties is an important element in conjugal success, but it is not the only element, and to make the general practitioner apparently the sole marriage counsellor argues too wide a view of the practitioner's functions and too restricted a view of marriage. If there is to be a recognized system of marriage guidance it will require not one counsellor but a whole board—doctor, priest, eugenist, economist, and perhaps several others, including, for the present at any rate, a house agent. Compulsory pre-marital medical examination, as one would expect, finds no acceptance. Apart from other objections, it would raise in an acute form the question of professional secrecy.

On the difficult matters of contraception and abortion P E P has much to say. It is of opinion that local authority clinics should not be limited to giving contraceptive advice to married women on medical grounds only, and that in principle such advice should be freely available, though it acknowledges that doctors in dealing with unmarried women may have to make exceptions in particular cases. In giving contraceptive advice generally doctors will help to foster the new attitude to parenthood without which a positive population policy based on democratic principles is bound to fail. As for abortion, the Interdepartmental Committee took the view that induced abortion could be justified for one reason only, to protect the woman's physical and mental health. The compilers of this report hold that the case for legalized induction, with the woman's consent, on certain eugenic grounds, especially of course having to do with mental defect, is very strong; but safeguards are necessary to prevent too wide an interpretation of "eugenic grounds." The most radical approach would be to make abortion available to every woman who desired it, provided there were no medical objections to the operation. It is recognized, however, that religious, ethical, and practical objections to the general legalization of abortion are much stronger than the objections to contraception. Contraception, unlike abortion, does not involve the actual destruction of human life.

This and other aspects of the population question must await further advances in medical knowledge and the crystallization of public opinion. The Minister of Health has recently stated in Parliament that the long-awaited report of the Royal Commission on Population may be completed this year, and it will be interesting to compare this with the P E P report. The latter can be commended for not losing sight of quality in pursuit of numbers, and for pleading not only for larger families but for a new attitude towards the family which should govern all discussion of social reform.

ACUTE PORPHYRIA

Failure to diagnose acute porphyria may lead to an unnecessary laparotomy in a seriously ill patient, and this undesirable error can be avoided only if the disease is considered as a possibility in the differential diagnosis of acute abdominal pain. Sudden onset of pain, with vomiting, constipation, and pronounced tachycardia, strongly suggests a surgical or gynaecological emergency (the patient is often a woman), especially when accompanied by guarding or rigidity in the lower quadrants of the abdomen, but when these signs and symptoms are due to acute porphyria doubt about the precise cause will usually arise. Abrahams, Gavey, and Maclagan[1] have observed that a urinary infection may also confuse the diagnosis. Elsewhere in this issue Dr. E. Petrie describes a case of acute porphyria and draws attention in his introductory remarks to the paucity of reports in British medical literature about this condition, which probably occurs more frequently than is generally realized.

The diagnosis can be firmly established only by examination of the urine, the appearance of which may be misleading in that the characteristic darkening to a port-wine colour does not appear if the urine is alkaline. Attacks frequently begin at the time of the menses, and coloration could be ascribed to contamination,[1] an error that may be increased by confusion between the absorption bands of haemoglobin and the zinc complex of porphyrin, which is probably the form in which porphyrin is always present in the urine in these cases. Provided due regard is paid to its distinction from urobilinogen, which may also be present, as Discombe and D'Silva[2] and others have found, the reaction of the urine with *p*-dimethylaminobenzaldehyde is apparently pathognomonic of the condition.[3]

Dr. Petrie's case is another example of the usual sequence of events which, curiously, are so "remarkably stereotyped." Symptoms and signs of central nervous involvement were present, with emphasis on the loss of motor function. In view of the fact that in affected individuals the condition is latent between attacks, or in others it may remain latent, it is obviously important to prevent them from taking drugs widely held to precipitate attacks. The drugs most incriminated are the barbiturates, sulphonal, and "trional." Hence the sedation of these patients, especially during the often-encountered phase of respiratory weakness, may become a difficult problem. Other substances also under suspicion are sulphonamides,[4] alcohol,[5] and lead, which sometimes all produce type III coproporphyrinuria in normal individuals. Recently Brunsting and Mason,[6] working at the Mayo Clinic, have made a careful study of four patients, all alcoholics, with hepatic impairment and lesions of the skin. Although the aetiology of this condition is obscure, the observations of these workers may lend support to the view, re-emphasized by Prunty[7] and based on other evidence, that the disease might be one of disordered hepatic metabolism. Other recent studies have raised doubt whether Waldenström's uroporphyrin III, found in this condition and held to be typical of acute porphyria, is in fact a chemical entity and not largely composed of uroporphyrin I.[7 8] This would be more in accord with the increasing number of reports of cases from the United States which combine features of both acute and congenital porphyria. Both conditions can still be regarded only as "inborn errors of metabolism," and elucidation of the nature of the errors still requires considerable biochemical investigation.

[1] *British Medical Journal*, 1947, **2**, 327.
[2] Ibid., 1945, **2**, 491.
[3] Watson, C. J., and Schwartz, S., *Proc. Soc. exp. Biol., N.Y.*, 1941, **47**, 393.
[4] Rimington, C., and Hemmings, A. W., *Biochem. J.*, 1939, **33**, 960.
[5] Watson, C. J., and Larson, E. A., *Physiol. Rev.*, 1947, **27**, 478.
[6] *Proc. Mayo Clin.*, 1947, **22**, 489.
[7] *Arch. intern. Med.*, 1946, **77**, 623.
[8] Watson, C. J., Schwartz, S., and Hawkinson, V., *J. biol. Chem.*, 1945, **157** 345.

NEUROMUSCULAR SYSTEM IN RHEUMATOID ARTHRITIS

The peripheral nerve symptoms in rheumatoid arthritis—muscle weakness and atrophy, numbness and paraesthesiae, and trophic changes in the skin—are features of the disease which led at one time to the belief that it originated in the central nervous system. This gave place to the view that an infection attacked the joints and that the other symptoms were secondary to this. Of recent years further research has shown that the joint symptoms are part of a general systemic disease and not the primary lesion. As far back as 1909 Llewellyn Jones[1] noticed that disturbed muscle function frequently preceded local evidence of joint disease, and this observation has received strong support from the demonstration by Steiner *et al.*[2] in the U.S.A., and by Gibson, Kersley, and Desmarais[3] in this country, of local accumulations of cells in the nerve sheaths and the interstitial tissue of the skeletal muscles. In the neighbourhood of these small and scattered lesions local degenerative changes affecting the axons and medullary sheaths of the nerves can be seen, and there is often extreme thinning of the muscle fibres accompanied by increase in the interstitial connective tissue.

Morrison, Short, Ludwig, and Schwab,[4] of the Harvard Medical School, have made an extensive investigation of the neuromuscular system in rheumatoid arthritis, using electro-myographic tracings and histological studies in a group of patients with well-marked rheumatoid arthritis. Patients with other forms of joint and muscle disease as well as healthy individuals formed a control series. They found no specific lesions in the central nervous system, but more pronounced alterations of the kind attributed to ageing than in controls of the same age. These changes were seen chiefly in the lateral projections of the anterior horns. Lesions were found in the peripheral nerves in 26 out of 31 cases and in the muscles in 8 out of 14 cases, thus confirming the findings of previous observers. Following careful research for involuntary muscle activity, fibrillation or fasciculation, spasticity, spread of tendon reflexes, voluntary and reflex muscle contractions, and neuromuscular influences in general, these workers concluded that lesions of the lower motor neurones were responsible for the muscle changes and neurological signs. Retrograde degenerative changes were found in the posterior root ganglia in several cases, confirming the observations of Penny[5] in 1913. In a very interesting case of arthritis affecting only one side certain reactions were noted in the forearm muscles of the opposite side, the joints then uninvolved. The following week the patient developed pain and arthritic signs in the unaffected hand—a very suggestive sequence of events.

[1] *Arthritis Deformans*, 1909. Bristol: John Wright.
[2] *Amer. J. Path.*, 1946, **22**, 103.
[3] *Ann. rheum. Dis.*, 1946, **5**, 131.
[4] *Amer. J. med. Sci.*, 1947, **214**, 33.
[5] *Bull. Comm. Study Spec. Dis.*, 1913, **4**, 43.

ACCOMMODATION AT ANNUAL MEETING

The accommodation at Cambridge for the Annual Meeting of the B.M.A. is limited. In order that the arrangements may run smoothly we would ask those who intend being present to notify the Executive Officer as soon as possible. The form for doing so appears at p. 123 of the *Supplement* this week.

MEDICINE IN THE 1939-45 WAR

REPORT OF MEDICAL RESEARCH COUNCIL

The Medical Research Council has gathered into a report running to 450 pages a brief account of the many-sided research which it sponsored or otherwise assisted during the war.[1] A vast amount of actual research was promoted by the Council, much of it with the object of supplying quick answers to newly emerged and urgent problems; it advised Government Departments and the Services on the application of scientific knowledge in the medical field, and it was responsible for many administrative tasks which a scientific organization was best fitted to carry out. Medical research in the war had three objects: (1) to maintain the health of the armed Forces and civil population, particularly by the prevention of infective diseases and malnutrition; (2) to advance all methods for rapid restoration of wounded and sick; and (3) to elucidate the conditions required for the highest possible efficiency of fighting personnel and industrial workers. The Council worked through 44 committees, in which advisers and experts of the greatest experience and ability were employed.

On almost every page of this report the reader will feel that he has read the same thing before. The bibliographies appended to the various sections make it seem that almost everything brought forward has already been the subject of a special publication or of a paper in a medical journal. The hand of the censor certainly did not lay heavy here. During the war 24 special reports of the Medical Research Council were issued; in addition there were 17 war memoranda, presenting a concise summary of current knowledge on subjects of urgent practical importance under war conditions. Innumerable papers were published from the National Institute for Medical Research and from the Council's external research establishments, over twenty in number. In the bibliographies in this report we find references to no fewer than 174 papers published during the war in the *British Medical Journal* alone, and there are many others in our more specialized contemporaries.

One of the Council's achievements was the *Bulletin of War Medicine*, in 60 parts, from September, 1940, to August, 1946, which formed an international exchange of medical information, especially for Service medical officers cut off from direct access to original publications The traditions of this wartime *Bulletin* are being maintained on an expanded basis by the new monthly abstracting journals brought out in the editorial department of the *British Medical Journal*.

Most of what appears in this report will be familiar, but it is useful to have it brought within a pair of covers in a readable and well-documented form. The following summary will remind readers of how much was done for medicine in this country by the Medical Research Council under the guidance of its secretary, Sir Edward Mellanby.

Wounds and Injuries

A War Wounds Committee was appointed by the Council during the campaign in Flanders and France in 1940, when, owing to the speed of the enemy's advance westward, large numbers of wounded had to be transferred to Britain before adequate surgical attention could be given to their injuries. This very large expert committee, with six subcommittees concerned respectively with anaerobic wound infections, burns, chest injuries, crush injuries, vascular injuries, and pathological specimens, worked under the chairmanship of the late Sir Cuthbert Wallace and later under that of Sir Ernest Rock Carling. Almost its first act was the publication of a pamphlet on the diagnosis and treatment of gas gangrene and the encouragement of the production of toxoids for the active immunization of troops against the more important clostridia of this disease. Gas gangrene, however, proved to be one of the rarest forms of wound infection, important only because of its severity and the danger it involved to life and limb. The study of the prevention and treatment of other types of wound infection was much wider in its scope and was attended by a very much higher degree of clinical success. The report reviews the development of wound treatment during the war, as exemplified particularly by the treatment of limb wounds in the British Army, and then summarizes current opinions of the uses and limitations of the sulphonamides and penicillin in the prevention and treatment of wound infection.

The following is given as a fair summary of current views on this last subject:

(1) Sulphonamide drugs, applied locally or given systemically (or both), are of only limited value in restraining the development of local infection in wounds, but are of definite value in preventing the systemic spread of streptococcal infection from a local focus such as a wound or burn. Both penicillin and the sulphonamides are effective in treating such systemic streptococcal infections on the rare occasions when these occur.

(2) The local use of sulphonamides will control infection by susceptible bacteria in superficial wounds; in deeper wounds these drugs, however administered, often fail to prevent or cure a local infection. The sulphonamides, used locally, are of value in preparing superficial wounds or burns for early skin-grafting, and penicillin, used locally, systemically, or both, is still better for this purpose.

(3) Penicillin has some outstanding advantages over the sulphonamides; it is effective against a wider range of Gram-positive bacteria, it is not antagonized by the presence of pus, it can be given systemically in large doses without serious danger of toxic effects, and it can be injected locally with less risk into body cavities. One of its comparative disadvantages is that it cannot economically be given by mouth. The combined use of penicillin injections and of sulphonamides by mouth has not been shown to give better prophylactic results against wound infection than the use of penicillin injections alone.

(4) Neither penicillin nor sulphonamide prophylaxis is a substitute for early and efficient primary surgical treatment of the wounded, but penicillin is a very valuable adjunct to surgery.

(5) Neither penicillin nor the sulphonamides will prevent the occasional development of gas gangrene in limbs deprived by injury of their blood supply and containing damaged and ischaemic muscle tissue.

(6) Neither penicillin nor sulphonamide therapy is effective against the Gram-negative bacteria which may infect wounds or burns at a relatively late stage (the stage of sloughing). For these cases alternative methods of treatment are necessary, of which irrigation with sodium hypochlorite solution is probably among the best at present available.

The report reviews the studies on hospital cross-infection, emergency amputations, and war fractures.

Burns, Brain and Nerve Injuries, etc.

A wide programme of research on the pathology and treatment of burns was sponsored by the Council during the war, and it soon became apparent that the problems of burns and their systemic effects were so manifold and complicated that an intensive system of co-ordinated laboratory and clinical research was required. Special reference is made to the experimental investigations in Prof. R. A. Peters's department at Oxford on "burns toxaemia" and the metabolic effects of burns; also to the work of the Burns Research Unit at Glasgow Royal Infirmary which led to the development of a first-aid cream containing penicillin and a sulphonamide drug for the elimination of streptococci. This preparation — "Glasgow No. 9 Cream," as it was called—was widely adopted for the treatment of Service and civilian casualties.

The Brain Injuries Committee, under the chairmanship of Prof. E. D. Adrian, examined the problems of the psychological state of patients after head injury, the relationship of head injury to subsequent epilepsy, the use of encephalography as a diagnostic measure, the prevention and treatment of headache and other complications, and the rehabilitation of brain-injured patients. Similarly a Nerve Injuries Committee, under Brigadier G. Riddoch, prepared memoranda on methods of testing for peripheral nerve lesions and the assessment of their recovery, and also sponsored investigations into the value of operative treatment for sciatica caused by prolapsed intervertebral disk.

Traumatic shock was the subject taken by another group, which surveyed the existing state of knowledge on that subject and directed the resumption of active research. A great volume of clinical, pathological, and experimental evidence regarding the different manifestations and treatments of shock due to wounds and burns was accumulated, but the compilers of the report say that there are many gaps in knowledge to

[1] *Medical Research in War. Report of the Medical Research Council for the Years 1939-45.* London: H.M. Stationery Office. 7s. 6d. net. Cmd. 7335.

be filled, and the implication of many of the more important studies made by British, American, and other workers during the war requires correlation.

"Thus the precise roles of haemorrhage, of plasma loss, of tissue damage, of associated biochemical changes, and of nervous influences in producing the altered haemodynamics causing acute illness after injury, require to be established and integrated; and the relationship of renal failure in the 'crush injury syndrome' to other forms of 'traumatic' and 'non-traumatic' anuria, and perhaps to the toxaemia deriving from the infective muscle necrosis of gas gangrene, has still to be fully elucidated."

But the main pieces of the puzzle have been fitted together, and if in peacetime the interest in the reactions of the body to injury can be maintained, and the opportunities for research afforded by traffic and industrial accidents can be effectively used, substantial advances may come in the near future.

War Diseases

The Council supported or co-ordinated important programmes of research concerning malaria, the typhus fevers, infective hepatitis and serum jaundice, and tuberculosis. The two outstanding contributions to medical research on malaria during the war period have been the effective introduction of malaria suppression by mepacrine and the synthesis by British workers of "paludrine." Mepacrine was strategically decisive in the overthrow of Japan, permitting military operations to be conducted successfully in hyperendemic malaria areas. The vast potential importance of D.D.T. as an insecticide and larvicide in malaria control must also be recognized.

In 1944 the Scrub Typhus Commission was set up, travelled to the headquarters of the Supreme Commander, South-East Asia, and undertook an active campaign to reduce the incidence of the disease, which had reached alarming proportions. A vaccine against scrub typhus was found to give a fair degree of protection to mice, and, although there was still lack of positive scientific evidence of protection in man, the position in the South-East Asia Command was so urgent that mass production of the vaccine was undertaken and the material sent out east. The sudden end of the war against Japan, however, prevented the assessment by the Army of the efficiency of the vaccine. Further field trials among civilian population have been organized, and the results, when available, should be of great interest.

The investigation of infective hepatitis proved most arduous. In spite of some promising results the transmission of the virus to animals has not yet been achieved with certainty. It was necessary to use human volunteers, and patients with rheumatoid arthritis were mostly chosen because it was known that the symptoms of that condition were sometimes relieved by an attack of jaundice. That was indeed borne out by the experiment, but the remission was only temporary; and it was clear that while jaundice was a useful research "tool" for the study of rheumatoid arthritis it could not be recommended as an effective treatment, and research on these lines was abandoned. The two most important discoveries made in connexion with this disease were that the virus is present in the blood of post-arsenical jaundice, and that the virus is excreted in the faeces in infective hepatitis. Without a susceptible animal, however, it is impossible to bring the research to the final goal of a prophylactic vaccine.

The report recounts the work done in wartime tuberculosis by the introduction of routine mass radiography, also the investigations on what is now recognized as a third mammalian type of tubercle bacillus—the murine type (the vole acid-fast bacillus). Plans for a field control to determine the prophylactic value in man of B.C.G. and of the vole bacillus are being considered.

Louse infestations were studied on a large scale, but with the advent of D.D.T., which played a large part in checking the Naples typhus epidemic, the troops engaged in the fighting on the Continent after D-Day were kept virtually free of lice. It is recalled that D.D.T. was first synthetized in 1874, but not until 1940 had its insecticidal properties been appreciated; and even then it was used only in Switzerland on a limited scale against agricultural pests. Not until early in 1943 was its large-scale production begun as an insecticide against one of the minor horrors of war. Scabies was also the subject of thorough investigation. The parasite was shown to be usually transmitted by intimate personal contact, and as a result the disinfestation of bedding has been given up by many progressive public health authorities, who now concentrate attention on the persons infested and their immediate contacts. It has been shown that when properly applied one treatment with benzyl benzoate emulsion will cure the disease in very nearly 100% of cases, so that disinfestation of clothing and bedding is unnecessary.

Development of Penicillin Therapy

Eighteen pages of this report are devoted to the history and development of penicillin therapy. The investigations on penicillin at the Sir William Dunn School of Pathology, Oxford, were supported by the Council from the beginning of the work which led to the introduction of penicillin into medicine as a chemotherapeutic agent. The early laboratory experiments at Oxford are narrated—the protective experiments in animals, the establishment of the "Oxford unit" of penicillin activity, the early efforts to increase production, the clinical trials, the use of penicillin in war wounds and burns (conditions which in the early stages had first priority at a time when the amount of penicillin available sufficed only to supply each of four centres with about 6 million units of penicillin monthly), and the gradually extending availability until by 1944, when the invasion of Normandy was about to begin, there was ample penicillin for all who needed it. By that time the Army Medical Service was able to organize on the widest possible scale prophylactic treatment against sepsis by parenteral injections beginning within 24 hours of wounding. The high quality of war surgery and the provision of penicillin reacted upon each other. Much of the success attending the use of penicillin was due to the very efficient surgery, and such surgery again received a stimulus because surgeons who were provided with penicillin were able to suture even the most severe wounds without the danger of major sepsis.

"Almost the whole of the work on which the present knowledge of penicillin therapy is based was done in Great Britain and the United States. Although penicillin was a British discovery, United States workers had the advantage of enormously greater supplies of the drug in its early years; study at many centres in America had begun before anyone outside Oxford had handled penicillin in England, and American output reached a spectacular level while ours was little more than a scanty trickle. Only when American penicillin was placed at the free disposal of our fighting Services was it possible for British clinicians to use it on an adequate scale. Nevertheless, it was in the early days of scarcity that the most substantial contributions to knowledge were made by British investigators, and these, almost without exception, were working on behalf of the Council."

The setting up of the Penicillin Clinical Trials Committee, under the chairmanship of Prof. H. R. Dean, is described. This committee was set up in the early part of 1943, its function being to increase knowledge of penicillin therapy by developing improved technical methods of administration and by extending the range of use of the drug to include conditions in which experience of its action was lacking; of these latter conditions many were caused by bacteria known to be susceptible *in vitro* to the action of penicillin. The committee had to steel its heart against humanitarian considerations because for many months the scarcity of penicillin was such that treatment had to be refused to cases in which it would no doubt have been beneficial but would not have advanced knowledge of the action of the drug. There was not nearly enough penicillin even to treat the cases of staphylococcal septicaemia which came to the committee's notice, and of all diseases this is the one which most imperatively demands penicillin treatment.

The most recent activity of the committee has been to investigate the treatment of subacute bacterial endocarditis on a scale large enough to provide information as to the system of dosage best suited to the disease. A preliminary report on this investigation (*British Medical Journal*, 1946, **1**, 381) showed clearly that while the scale of penicillin dosage appropriate to diseases other than subacute bacterial endocarditis is usually ineffective in that condition the administration of larger doses for 28 days or more can almost always cure it in its early stages.

The Wartime Drug Position

Some interesting history is contained in the section of the report which deals with the drug position in wartime. Those

who recall the 1914–18 war will remember that a serious position arose owing to the shortage of certain drugs the supply of which up to then had been forthcoming from German chemical houses. In 1939 steps had been taken to ensure an accumulation of adequate stocks of natural and synthetic medicaments of foreign origin. The large-scale manufacture and supply of certain antitoxins and other immunological products for which there was likely to be a heavy demand under war conditions was also undertaken. British equivalents of the more important synthetic drugs and diagnostic agents hitherto obtainable only from enemy countries were manufactured here, and when considered advisable—that is, when the chemical identity of the British substitute with its foreign prototype was not entirely obvious—were submitted to special clinical trials. Thus mepacrine was substituted for the German "atebrin," pamaquin for "plasmoquine," bromethol for "avertin," soluble hexobarbitone for "evipan sodium," iodoxyl for "uroselectan-B," pheniodol for "biliselectan," and pethidine for "dolantin" or "dolantol," a synthetic substitute for morphine.

A Therapeutic Requirements Committee was set up under the chairmanship of Prof. L. J. Witts, on which the three bodies already producing official drug formularies were represented—namely, the Pharmacopoeia Commission, responsible for the *British Pharmacopoeia*; the Pharmaceutical Society, for the *British Pharmaceutical Codex*; and the Insurance Acts Committee of the British Medical Association, for the *National Formulary*. The functions of this committee were to advise the controllers of the import and manufacture of drugs which drugs were vitally necessary and must be supplied at all costs. It informed the medical profession, more particularly the key people responsible for formularies, indents, and quotas, which important drugs were scarce and must be used economically. Generally it dealt with the problems which inevitably arise when any form of restriction is practised. Instances are given of the changes in therapy which gave rise to supply problems of varying degrees of complexity, such as the replacement of sulphur by benzyl benzoate in the treatment of scabies, the replacement of tannic acid by sulphonamides and penicillin in the treatment of burns, the sequence of safrol, lethane, and finally D.D.T. in the treatment of louse infestation, and the series thiourea, thiouracil, and methyl thiouracil in the treatment of hyperthyroidism.

"The more permanent effects on prescribing produced by the Committee's activities during the war remain a subject for speculation. In general, they were the acceleration of changes which would have come more gradually in peacetime, an acceleration which was the result of expert direction and the avoidance of vested interests or unsupported tradition. Single substances and active principles were used instead of tinctures and mixtures; the many hospital pharmacopoeias, which are chiefly of historical interest, were replaced by the *National War Formulary* of the Ministry of Health, and the use of foreign or proprietary names was discouraged. Synthetic chemicals were substituted for galenical drugs. Bismuth salts gave way to magnesium trisilicate and aluminium hydroxide in the treatment of dyspepsia, boric lint was replaced by the sulphonamides and penicillin. Production of needless varieties of hypnotics and local anaesthetics was temporarily checked. Finally . . . a demand was created for disinterested accounts of the increasingly rapid developments and changes in pharmacology, and their scientific application to the practice of medicine."

The Drug Requirements Committee recently appointed by the Ministry of Health has now taken over the functions, as applied to post-war conditions, of the Therapeutic Requirements Committee, which was discharged on the completion of its wartime task.

Nutritional Standards

A full account is given of the manner in which rationing was introduced, the nutritional investigations which preceded it, and the work which led to a recasting of Service rations and rations for special troops and for tropical climates. In 1943 a committee was appointed under the chairmanship of Dr. A. N. Drury to obtain evidence of the nutritional state of the people in the fourth year of war. The main index of the nutritional state was taken to be the haemoglobin content of the blood. Haemoglobin levels of 13,000 adults and 3,000 children were determined, as well as a smaller number of serum protein estimations as a subsidiary index. From these it was concluded that the general situation was reasonably good, though an effort was made to improve still further the haemoglobin levels of young children, pregnant women, and the poorer members of the population.

The work of the Accessory Food Factors Committee was concerned with the composition of wartime bread and the vitamin content of various foodstuffs, but the work of the Food Rationing (Special Diets) Committee, with Sir Edward Mellanby as its chairman, was the most exacting and difficult of all. This committee had the task of organizing food rationing for invalids. It received, as was to be expected, innumerable special applications for extra rations, often from sufferers from rare diseases or from variants of illnesses for which extra rations had already been refused. Each case was considered individually, specialist advice was sought where necessary, and a written statement was made of the reasons for or against granting extra rations. The body of rulings which accumulated from these decisions came to play an important part in the system of rationing. The committee must often have been gravely troubled when it came to deciding the order of priority in the claims of invalids for extra rations when the humanitarian impulse was to grant them all if only there was a sufficiency of food available. Certain principles were laid down: that extra rations should be granted only on the grounds of therapeutic necessity; that in deciding between competing claims preference should be given to those invalids with better chances of recovery or those who required special rations to maintain active health; and that extra rations should not be allowed for the construction of those traditional dietaries for invalids and convalescents which, however comforting to the patient, are without known effect on the ultimate outcome of his disease. The heartburning and the depression which must have resulted among invalids and their doctors as a result of these decisions can be imagined; but the nation was at war, and civilians, including invalids and convalescents, were in the front line in more senses than one. Except for an extra allowance of tea to the elderly, they, with hopeless invalids, the insane, and the mentally and physically defective, were denied any concessions unless they suffered from another condition which itself qualified for extra rations.

Special Diet Problems

As a result of seven years of rationing a unique experience was acquired of rationing as applied to invalids. Some of these results are set out. A generous allowance of fat was provided to meet the needs of diabetics because, by greatly restricting their intake of carbohydrate and substituting fat, they can avoid or restrict the use of insulin. Patients with pernicious anaemia were as a rule refused fresh liver, because experience has shown that treatment with fresh liver is far less efficient than the parenteral injection of liver extract. Fresh liver was allowed only where there was a supposed sensitivity to the extracts.

Patients with tuberculosis had been accustomed to receive a full diet, particularly one rich in fats. Certain studies undertaken just before rationing began to be severe showed, however, that fat had no advantage over carbohydrate; also that after two to three months on a high-fat diet the appetites of tuberculous patients declined and their weights fell, effects not observed on a high-carbohydrate diet. Carbohydrates being available in ample quantities, the committee held a watching brief, and after further inquiries and reports the only special rations allowed in tuberculosis were 2 pints of liquid milk daily in active—i.e., unhealed—tuberculosis, and later, when the cooking-fat ration was reduced, supplies to these patients were continued at the previous level.

An outbreak of alleged "food sensitivity" following the institution of rationing caused a good deal of trouble. As soon as it was announced that butter was to be rationed, innumerable margarine-sensitive people made application for extra butter, but the number of applications declined abruptly as soon as it was known that these people would be put through a test requiring them to distinguish margarine from butter when the taste was disguised. Similar complaints of sensitivity coincided with—in some cases actually anticipated—changes in the type of flour. Tests here gave little support for the view that persons can be sensitive to National flour but insensitive to white flour. Applications were made for condensed milk because of alleged sensitivity to raw cow's milk. In such cases the applicant's doctor was advised to order the milk to be boiled, and the measure appeared usually to suffice.

The proposal to add calcium carbonate to National flour evoked a storm of protest. Diverse ill effects, ranging from the development of arteriosclerosis to nephrolithiasis, were predicted. One eminent physician wrote alleging that he and his whole family were being poisoned by the added calcium, whereas calcium salts were first added to the flour three months after the receipt of his letter! Actually the amount of calcium added to flour was hardly more than that needed to compensate for the amount of phytic acid it contained.

The Special Diets Committee is now anticipating the period of derationing, though it is already evident that any amelioration in the food supply position will develop slowly and piecemeal. But plans should be laid in advance so that, with increase of supplies, distribution can be made to the best advantage. All the conditions for which extra rations have been refused have been analysed and classified according to the order of priority in which the refusals should be rescinded. This is good news for chronic invalids and perhaps also for those people who have a sensitivity for certain foods, even though in the view of the experts such sensitivity is more imagined than real.

Various Emergency Services

A section of this report is allotted to what is called "Personnel Research," chiefly in connexion with the fighting services. This included studies of suitable clothing or armour for fighting men in widely different environments, and of the physiological and psychological adjustments which it is possible to make to hazards and unusual situations. Health research in industry was undertaken by the Industrial Health Research Board, and included studies in ventilation and air hygiene, lighting, industrial psychology, and diseases due to inhaled dusts or poisonous fumes.

Among the emergency services set up was one for the co-ordination of the supplies of serological products and the provision of large stocks of polyvalent gas-gangrene antitoxin and reserve supplies of a number of vaccines and sera. The emergency public health laboratory service has been placed on a permanent basis to meet peace-time calls. In this service during the war special studies were made of non-pulmonary tuberculosis, cerebrospinal meningitis, and cross-infection in hospital wards.

The organization of the blood transfusion service called for careful planning. The four London emergency blood supply depots, situated at Luton, Maidstone, Sutton, and Slough, enrolled 128,320 donors during the five years of war. Research was also carried out on precise methods of blood grouping, on the rare accidents which followed transfusion, and on the possible risk of post-transfusion jaundice and the measures to be taken to meet it. Another activity was the setting up of a hospitals radon centre at Barton in Bedfordshire, where the radon plant, in view of the danger of the dispersal of radioactive substances by enemy action, was kept in safety in deep caves. Radium was lent to the centre by the Radium Commission and by St. Bartholomew's, and the three radon plants at Barton dealt with about 9,500 requests for radon for use in treatment or research.

Many Research Teams

The remainder of the report is a summary of the work done by each of several institutions—the National Institute for Medical Research, twenty or so external establishments, permanent or semi-permanent, the temporary units, and other research groups. At the central institute at Hampstead and the laboratories at Mill Hill work was done on problems connected with traumatic shock, underwater physiology, influenza (a continuing research throughout the war), air-borne infections, the chemotherapy of virus diseases, anaerobic and other wound infections, immunization against tetanus, diphtheria, and gas gangrene, and on certain problems in biophysics and physical chemistry. Here also much work was done on biological standards. Three new standards were provided and made available at Hampstead during the war—those for vitamin E, heparin, and penicillin. An out-station of the National Institute was the Common Cold Research Unit at Salisbury.

In the Departments of Clinical Research at University College and Guy's studies were made of the symptoms of shock in air-raid casualties. At the Neurological Research Unit at Queen Square various factors connected with high altitude flying were investigated. At the Otological Unit at the same hospital work was done on deafness and hearing-aids. The Birmingham Accident Hospital had a unit concerned with the epidemiology, prevention, and treatment of wound infection, and at the same hospital and at the Glasgow Royal Infirmary other units studied the control of infection in burns and scalds. In a research unit at Hammersmith Hospital an experimental comparison was made between gamma rays and *x* rays in the treatment of cancer of the mouth and throat; a full report of this experiment has been prepared for publication. Important dietary studies were carried out in the Department of Experimental Medicine at Cambridge, at the Nutrition Building at Mill Hill, and at the Human Nutrition Research Unit at the National Hospital, Queen Square. At the Dunn Nutritional Laboratory, Cambridge, an analysis was made of fortified products such as vitaminized margarine and special food preparations. Several establishments were devoted to research on health in industry, notably the Department for Research in Industrial Medicine at London Hospital, the Applied Physiological Research Unit at Cambridge, and the Industrial Physiology Department at the London School of Hygiene and Tropical Medicine. At the London School also the effects of bombing on the civilian population and the protective value of shelters and other precautionary measures were studied.

The special work on diseases of children carried out by members of the Council's staff at the Queen Elizabeth Hospital for Children, London; on the pathology of the nervous system at the London Hospital; on biologically effective radiation at the Strangeways Research Laboratory, Cambridge—these and many other investigations deserve permanent record. About 250 special investigations by outside workers, individuals or small teams, were supported by grants from the Council.

The main burden of the editorship of this well-compiled report has fallen upon Dr. F. H. K. Green, formerly Publications Officer, and now Assistant Secretary of the Council.

PUBLIC HEALTH CENTENARY

To commemorate the centenary of the Public Health Act, 1848, and in particular the appointment of Sir John Simon as the first medical officer of health for the City of London, the Lord Mayor and Corporation gave a dinner at Guildhall on May 7. The Minister of Health, Mr. Aneurin Bevan, was present with three of his predecessors, Lord Addison, the first Minister of Health, Lord Kennet (formerly Sir Hilton Young), and Mr. Ernest Brown. With the help of the archivist of the City a series of exhibits was arranged illustrating the Corporation's interest in public health, especially in water supply, cleansing of streets, and abatement of grosser nuisances, as far back as the thirteenth century.

Mr. Aneurin Bevan proposed "The Pioneers of Public Health." The task which the reformers had faced in 1848, he said, was formidable. They were opposed by many vested interests. "Property and bumbledom fought together to deny the child the right to live." No one at that time thought public health a good investment. Even the great political figures of the day withheld their support from this cause. John Bright spoke only once on this subject, and that was to oppose a measure of smoke abatement. The pioneers whom Mr. Bevan asked the company to honour were Edwin Chadwick, John Simon, and William Farr. Chadwick fearlessly made public the conditions under which the industrial population was existing, and in doing so incurred much enmity. John Simon, who after seven years in the City became medical officer of the Central Board of Health, then medical officer of the Privy Council, and finally first medical officer of the new Local Government Board, designed many administrative measures to alleviate social evils. William Farr, the statistician, might be described as the first to show the advantage of a Government scheme of national health insurance, and in his unceasing efforts for preventive medicine this son of a farm labourer had been a source of inspiration right down to our own time. To these names Mr. Bevan added the name of one politician, Lord Morpeth, afterwards Earl of Carlisle, who introduced the Public Health Bill in 1848.

Sir George Elliston, chairman of the Public Health Committee, proposed the health of the guests, to which the first of three responses was made by Lord Addison. Lord Addison recalled that with the assistance of the late Sir Robert Morant and Sir George Newman he was called upon to draft the proposals relating to maternity and child welfare which found their place in the budget of 1914. So much was the new service appreciated that early in 1917 a committee was set up consisting of Lord Milner, Mr. Arthur Henderson, Mrs. Beatrice Webb, and himself to consider the question of the establishment of a Ministry of Health. It took only two weeks to arrive at a unanimous report, but difficulties arose when it came to the actual establishment of the Ministry, and terms had to be made with local authorities and approved societies, so that not until 1918 was blessing formally given to the project. He became the first Minister in 1919, and was succeeded by Lord Melchett in 1921.

Responses were also made by the Bishop of London, who spoke of the function of the Church in the field of public health, and by Sir Alfred Webb-Johnson, who reminded the company that Sir John Simon was not only a pioneer in public health but a great surgeon, and indeed one of his predecessors in the presidency of the Royal College. Sir Alfred touched lightly upon present or subsiding controversies, as did Lord Balfour of Burleigh, chairman of the Medical Research Council, who wished godspeed to the Minister and to the medical profession in their endeavours to bring in the new health service. Lord Balfour proposed the health of the Corporation, and the Lord Mayor (Sir F. Michael Wells) replied.

SEA AND AIR PORT HEALTH AUTHORITIES

ANNUAL CONFERENCE

The forty-ninth annual conference of the Association of Sea and Air Port Health Authorities of the British Isles was held at Swansea on May 12, 13, and 14, under the presidency of Councillor William Evans, chairman of the Swansea Port Health Committee. The delegates were welcomed by the Mayor, Councillor Sir William A. Jenkins, J.P. At the annual general meeting held on the first morning of the conference Alderman T. F. Mooney, of Newport, was elected president for the year 1948–9. Dr. H. C. Maurice Williams, of Southampton, was re-elected honorary secretary, and Dr. W. M. Frazer, of Liverpool, honorary treasurer.

Golden Jubilee

To mark the Association's fiftieth jubilee, Dr. Nicolas Gebbie, port medical officer to the Hull and Goole Port Health Authority, gave an address entitled, "The Romance of the Port Health Service and of its Association." The idea of forming the Association, he said, was conceived by the Hull and Goole Port Sanitary Authority, which with other authorities realized that concerted action was needed to safeguard the health of seafarers. The first president was Dr. Fraser, a general practitioner and chairman of the Hull and Goole authority. Dr. Gebbie described the work carried out by port health authorities, and he reminded the conference that a further problem had developed during recent years—namely, the prevention of the introduction of infectious disease by air traffic. He discussed some of the early outbreaks of cholera in this country. The disease was unknown outside Asia until 1817: it subsequently spread to the West in four great waves, reaching Europe along the four main lines of travel from India: through Afghanistan and the caravan routes to Russia; by the Gulf of Persia to Syria and Egypt, and across the Caspian to Russia: by the pilgrim traffic to the Red Sea, thence to Egypt and the Mediterranean; and by the Trans-Caspian railway and the Caspian steamers to Russia. The infection came to England usually from Russia and Germany through the North Sea ports—for example, Sunderland and Newcastle in 1831, and Glasgow and London in 1832. In the 1831–2 epidemic there were 21,000 deaths in England and 9,000 deaths in Scotland. Further epidemics affected England in 1848–9, in 1854, and in 1865–6. The Prudential Assurance Company was founded by a Lambeth clergyman to insure his parishioners against cholera during the 1854 outbreak.

Port sanitary authorities were the first line of defence against cholera, and their defence was strengthened by the formation of their Association in 1898. The work of the Association had extended with that of its constituent authorities, and its advice had been sought on many occasions by national and other bodies.

Naval Hygiene

Surgeon-Captain Hugh M. Willoughby, deputy medical officer of health, Port of London, described his experiences as a hygiene officer in the Royal Navy at Alexandria. During his first two years in the Eastern Mediterranean there was no major epidemic of infectious disease. A few cases of dysentery occurred, but the incidence was kept low owing, in his opinion, to the ban on the eating of salads, melons, and fruit such as strawberries. Referring to "gyppy tummy," the speaker considered bacteriophage useful both as a prophylactic and in treatment provided that it was made from a local strain of the infective agent.

The incidence of malaria was low. There were only 29 cases reported during 1940, the majority infected in Crete and Greece. One of the greatest problems was supplying fresh water to Tobruk. All fresh water had to be conveyed in carriers previously used as oil and petrol tankers. Owing to good propaganda and recreational facilities, the incidence of venereal diseases in Alexandria was lower than in any home port in England.

Cholera in Egypt

Dr. R. Barrett, of the Ministry of Health, read a paper on the Egyptian cholera outbreak of 1947 and its effect on civil aviation. Egypt had suffered two epidemics of cholera in the past century. The first, in 1902, resulted in 34,000 deaths in a population of 5 millions. This epidemic was traced to the clandestine return of pilgrims from Mecca. Egypt had always been a centre of international sea and land traffic, and was now also an important centre of air traffic. Air routes radiated from Cairo to all parts of Europe, Asia and the Far East, Australia, New Zealand, Africa, and North and South America.

For climatic and economic reasons Egypt was a country where at certain seasons cholera could develop in epidemic form. Its sudden reappearance in 1947 caused considerable anxiety. This epidemic appeared to have no connexion with the pilgrimage to Mecca. The first cases were notified as food-poisoning and occurred in a native village with a primitive sewerage system and a water supply that came from a shallow well. The main occupation of the inhabitants consisted of cultivating dates, pressing them into cakes, and selling them to other villages in Lower Egypt. In spite of immediate precautions the disease spread to the neighbouring villages and provinces, until all the provinces in Upper and Lower Egypt, with one exception, were reporting cases of cholera. The last case was reported on Dec. 31, 1947, and six weeks later Egypt declared herself free from cholera. The total number of deaths in the outbreak was 10,383 in a population of 10 millions. It was significant that the disease did not get a hold in any of the cities where water supplies and sewerage systems were of modern design. The Egyptian Government took elaborate precautions to prevent the epidemic from spreading.

Dr. Barrett said that it was a matter for speculation whether the epidemic ended as a result of the seasonal drop in atmospheric humidity and the fall in temperature or because of the preventive measures introduced. The need for international agreement on measures for the sanitary control of aerial navigation was well demonstrated by this epidemic.

Aircraft having a case of cholera on board must undergo medical inspection, isolation of the sick, and surveillance of passengers and crew for five days (the internationally agreed incubation period), disinfection of passenger effects and parts of the aircraft, and disinfection of the drinking water. Medical inspection of all passengers and crew and surveillance for five days was also prescribed for any aircraft from an infected area. Only in one instance was a suspected case of cholera reported in an aircraft, at Darwin, and that was not confirmed bacteriologically. The only measures, therefore, that should have been imposed on any other aircraft or passengers were medical

inspection and surveillance. In fact, during the time of the epidemics seven countries closed their frontiers to air traffic from Egypt. Another stopped air traffic to Egypt in order to have time to equip her airports to deal with any cases of cholera. Others restricted air traffic to one airfield.

Inoculations against cholera did not provide absolute protection, and therefore inoculated passengers were still subject to surveillance under the Conventions. The procedure adopted for inoculation varied, some countries insisting on two inoculations, others requiring certificates to state the number of vibrios injected. Two countries insisted that all travellers from Egypt should be detained en route for a period of seven to eight days, and both these countries insisted upon negative stool examinations before entering. The effects, therefore, on air services were severe, and many of the countries introduced measures outside the scope of the requirements of the International Conventions. Such difficulties did not normally arise with maritime traffic, and this was a problem for which both Governments and airlines would have to find a solution. He suggested that there should be a standard procedure and that the vaccine should be standardized, as in the case of yellow fever.

During the conference the delegates visited several places of interest, including docks at Swansea and Port Talbot, the National Oil Refinery, Skewen, the Metal Box Factory at Neath, and the Imperial Chemical Industries Works at Waunarlwydd.

NATIONAL HEALTH SERVICE

DESIGNATION OF LONDON TEACHING HOSPITALS

Mr. Aneurin Bevan, the Minister of Health, has made the National Health Service (Designation of Teaching Hospitals, No. 2)* Order, 1948, under the provisions of the National Health Service Act, 1946, designating 26 teaching hospitals in the London area. The 26 designated hospitals comprise a total of approximately 60 constituent hospitals. The names of all the hospitals concerned are given in the Order.

Each designated teaching hospital will be administered by a new Board of Governors, who will shortly be appointed by the Minister when he has considered the nominations and recommendations of various authorities and organizations who are concerned.

The teaching hospitals so designated under the Act have been given a separate identity and status, and in addition to their primary function of treating the sick they will provide facilities for clinical teaching and research in accordance with the needs of the undergraduate medical and dental schools and postgraduate institutes of the University of London.

As the group comprising each teaching hospital will be one entity for formal administration it has been necessary in some cases to give it a new title. But the Minister would wish the names of the constituent hospitals, many of which are of long standing and have valuable associations and traditions, still to be used for everyday purposes.

The first Order, made early in April, designated Teaching Hospitals in the Provinces.

Title (1)	*Hospital or Group of Hospitals* (2)
The Royal Hospital of St. Bartholomew	The Royal Hospital of St. Bartholomew, E.C.1 (including the Alexandra Hospital for Children with Hip Disease, and the Zachary Merton Convalescent Home, Northwood).
The London Hospital	The London Hospital, E.1 (including the Croft Home, Reigate, the Marie Celeste Annexe, Reigate, the Zachary Merton Annexe, Banstead, the London Hospital Annexe, Brentwood, and the Herman de Stern Convalescent Home, Felixstowe). Queen Mary's Maternity Home, Hampstead, N.W.3.
The Royal Free Hospital	The Royal Free Hospital W.C.1 (excluding the Eastman Dental Clinic). The London Fever Hospital, N.1. The Elizabeth Garrett Anderson Hospital, N.W.1 (including the Rosa Morrison House, New Barnet, and the Garrett Anderson Hospital Maternity Home, Belsize Grove). The Hampstead General Hospital and North-West London General Hospital, N.W.3. The Children's Hospital, Hampstead, N.W.3. The North-Western Hospital (L.C.C.), Hampstead, N.W.3.
University College Hospital	The North London or University College Hospital, W.C.1 (including the Obstetric Hospital and the Royal Ear Hospital, Huntley Street, W.C.1). The Hospital for Tropical Diseases, W.1. St. Pancras Hospital (L.C.C.), N.W.1.
The Middlesex Hospital	The Middlesex Hospital and Cancer Wing, W.1 (including the Middlesex Branch Hospital and Hulke Endowed Convalescent Home, Clacton-on-Sea). The Woodside Hospital for Functional Nervous Disorders, N.10 (including the Country Branch, Welders House, Chalfont St. Peter, Bucks). The Hospital for Women, Soho Square, W.1. The British Red Cross Society's Clinic for Rheumatism, Peto Place, N.W.1.
Charing Cross Hospital	Charing Cross Hospital, W.C.2. Harrow Hospital, Roxeth Park, Harrow-on-the-Hill. Wembley Hospital, Fairview Avenue, Wembley.
St. George's Hospital	St. George's Hospital, Hyde Park Corner (including the Atkinson Morley Convalescent Hospital, Wimbledon). The Victoria Hospital for Children, S.W.3 (including the Victoria Convalescent Home, Broadstairs). The Princess Beatrice Hospital, S.W.5. The Royal Dental Hospital of London, W.C.2.
Westminster Hospital	Westminster Hospital, S.W.1 (including the Westminster Hospital Convalescent Home, Chartham Park, Sussex, the Westminster Hospital (Parkwood) Convalescent Home, Swanley, Kent, and the Yarrow Home of Westminster Hospital, for Convalescent Children, Broadstairs, Kent). The Infants Hospital, S.W.1. The Gordon Hospital for Diseases of the Rectum and Colon, S.W.1. All Saints Hospital, S.E.11.
St. Mary's Hospital	St. Mary's Hospital, W.2 (including Joyce Grove House, Nettlebed, Oxon., and Adair Lodge, Aldeburgh). Paddington Green Children's Hospital, W.2 (including the "Clear Springs" Convalescent Home and the "Pinecroft" Convalescent Home, Lightwater, Surrey). The Princess Louise Kensington Hospital for Children, W.10 (including the Convalescent Home, 19–20, South Terrace, Littlehampton). The Samaritan Free Hospital for Women, N.W.1. The Western Ophthalmic Hospital, N.W.1. St. Luke's Hospital for Advanced Cases, W.2.
Guy's Hospital	Guy's Hospital, S.E.1 (including the York Clinic, Nuffield House, and "Holmesdale," Nutfield, Surrey). The Evelina Hospital for Sick Children, S.E.1 (including the Eleanor Wemyss Recovery and Convalescent Home, Crazies Hill, near Reading).

*Statutory Instruments, 1948, No. 979: National Health Service (Designation of Teaching Hospitals (No. 2) Order). H.M.S.O., price 1d., post free 2d

Title (1)	*Hospital or Group of Hospitals* (2)
King's College Hospital	King's College Hospital, S.E.5 (including the Baldwin Brown Convalescent Home, Camberley). The Royal Eye Hospital or Royal South London Ophthalmic Hospital, S.E.1 (including the Royal Eye Hospital Branch, Surbiton). The Belgrave Hospital for Children (including the Belgrave Hospital Convalescent Home, Minstead, Hants).
St. Thomas's Hospital	St. Thomas's Hospital, S.E.1. The Royal Waterloo Hospital for Children and Women, S.E.1. The General Lying-in Hospital, S.E.1. The Grosvenor Hospital for Women, S.W.1. The Roffey Park Rehabilitation Centre, Horsham, Sussex.
The Hammersmith, West London, and St. Mark's Hospitals	Hammersmith Hospital, W.12. West London Hospital, W.6. St. Mark's Hospital for Cancer, Fistula, and Other Diseases of the Rectum, E.C.1.
The Hospital for Sick Children	The Hospital for Sick Children, W.C.1 (including the Tadworth Court Branch Hospital, Tadworth, Surrey, "Runabouts" Convalescent Home, Chipping Norton, Oxon., and the Sarah Louise Convalescent Home, Hove, Sussex).
The National Hospitals for Nervous Diseases	The National Hospital, Queen Square, W.C.1 (including the National Hospital Convalescent Home, Finchley). The Maida Vale Hospital for Nervous Diseases, W.9.
The Royal National Throat, Nose and Ear Hospital	The Royal National Throat, Nose and Ear Hospital (including the Central London Hospital Division, W.C.1, the Golden Square Hospital Division, W.1, and the Dame Gertrude Young Memorial Convalescent Home, Castle Bar Hill, W.5).
The Moorfields Westminster and Central Eye Hospital	The Moorfields Westminster and Central Eye Hospital.
The Bethlem and Maudsley Hospital	The Bethlem Royal Hospital for Nervous and Mental Disorders, Beckenham. The Maudsley Hospital, S.E.5.
St. John's Hospital for Diseases of the Skin	St. John's Hospital for Diseases of the Skin, W.C.2.
The Hospitals for Diseases of the Chest	The Hospital for Consumption and Diseases of the Chest, S.W.3 (including the Brompton Hospital Sanatorium, Frimley, Hants). The London Chest Hospital, E.2 (including the London Chest Hospital Annexe, Arlesey, Beds).
The Royal National Orthopaedic Hospital	The Royal National Orthopaedic Hospital, W.1 (including the Country Branch and Convalescent Branch, Stanmore).
The National Heart Hospital	The National Hospital for Diseases of the Heart, W.1 (including the Country Branch, Maid's Moreton, Bucks).
St. Peter's and St. Paul's Hospitals	St. Peter's Hospital for Stone and Other Urinary Diseases, W.C.2. St. Paul's Hospital for Urological and Skin Diseases, W.C.2.
The Royal Cancer Hospital	The Royal Cancer Hospital (Free), S.W.3.
Queen Charlotte's and Chelsea Hospitals	Queen Charlotte's Maternity Hospital, W.6. The Chelsea Hospital for Women, S.W.3 (including the Chelsea Hospital Convalescent Home, St. Leonard's-on-Sea).
The Eastman Dental Clinic	The Eastman Dental Clinic, W.C.1.

Reports of Societies

GENERALIZED DISEASES OF BONE

At a meeting of the Section of Medicine of the Royal Society of Medicine on April 27, Dr. MAURICE DAVIDSON presiding, the subject presented was generalized disease of bone in adults. There was no general discussion.

Dr. E. F. SCOWEN spoke of the effect of endocrine disorders on bone diseases. Wherever bone was formed the final part of the story must be the formation of a matrix which later became calcified. In the first place there might be a normal or an excessive quantity of matrix formed which might be irregularly calcified or not calcified at all—a condition arising from a disturbance of calcium or phosphorus metabolism. Another condition might arise from excessive resorption of bone even though bone formation was proceeding normally. Lastly, there might be failure of formation of the osseous matrix. This might not be complete, and, if partial, such bone as was formed might be formed normally and calcify normally, so that a condition of osteoporosis occurred. Dr. Scowen proceeded to show a number of photographs and radiographs illustrating endocrine abnormalities as reflected in bone changes. Certain changes seen in acromegaly had received little attention. In the thoracic spine irregular new bone formation might be seen, with decalcification behind it, giving rise to a curious appearance when the spine was viewed as a whole, the thoracic vertebrae appearing very much larger than the upper lumbar vertebrae. In the adult as a result of the stimulation of excessive bone production the vertebrae were still capable of producing a good deal of new bone, but such formation was often localized to the middle and lower thoracic vertebrae.

Method of Classification

Dr. J. F. BRAILSFORD said that the conditions which led to generalized diseases of bone might be grouped under five headings: (1) dysplasias and dystrophies which began in foetal or infantile life, and were of varying severity, some being incompatible with the continuance of life, while others were so slight that the victim survived into old age and the condition was discovered only incidentally on some radiographic examination; (2) generalized conditions of bone due to disturbance in some other organ—for example, renal disease; (3) generalized diseases of bone due to deficiencies and endocrine and blood disorders, for example, osteomalacia, hyperparathyroidism, anaemia, or leukaemia; (4) conditions which attracted attention during the major part of the illness only by the occurrence of a local lesion; and (5) a group of conditions in which the patient, who had been perfectly well, began to have pain and aching in the limbs, but for a year or even two years without perceptible radiographic changes—a group including syphilis and carcinomatosis. Dr. Brailsford suggested that the radiography of the hand facilitated the separation of these generalized conditions from conditions which, for the most part localized, gradually spread to other bones. Radiologically two types of reaction were seen, namely, the reaction which brought about a diminished density of the bone and the reaction which produced an increased density. In some conditions both reactions occurred, one after the other. By using the classification he had given he thought that these generalized diseases of the skeleton could be put into something like order.

It had been stated that hyperparathyroidism was a condition which in the majority of cases revealed itself by renal complications. That had not been his experience. The most striking feature was decalcification of the terminal phalanges, absence of compact tissue, and the formation of cysts in one or two of the bones. The formation of cysts in that type of osteoporosis was not seen in the same way in any other condition. Only one condition approached it, namely, severe renal osteodystrophy, in which there was a history projected from childhood into the later years of life, with bones which had been deformed very early in life. In hyperparathyroidism the architecture of normal bone was presented, apart from lack of compact tissue whereas in renal osteodystrophy there was likely to be deformity.

The characteristic feature of Paget's disease, which began as a localized lesion, was the tearing away in a V-shaped fashion of the periosteum from the adjacent living bone. Paget's disease might involve every bone in the skeleton, but normally this was not so. It might be that the head, spine, pelvis, and femur were extensively involved, yet on examining the bones of the hand only one metacarpal might be found affected, the rest of the bones being normal.

Sir HAROLD FAIRBANK referred to some unusual cases. Osteogenesis imperfecta might, for example, be of interest in an adult patient. One severe case, pre-natal in origin, was in a girl who never walked at all until 12 years of age, and sustained many fractures later on; she was now a dwarf aged 31, but was able to get about and carry on office work. A woman of 72 with "marble bone" was admitted to hospital with a minor head injury, and only then was the extreme density of the bones discovered. She had carried on for many years with practically no bone marrow at all. As an example of endocrine disorders he described the case of an intelligent well-proportioned dwarf of 46, most of whose epiphyses were still ununited, and the radiographs of whose skull showed what was apparently a partially calcified cyst of the pituitary.

ABDOMINAL PAIN

At a meeting of the Manchester Medical Society on April 7 Prof. JOHN MORLEY delivered his presidential address—"Second Thoughts on Abdominal Pain."

He recalled that the thesis he had advanced in 1931 followed James Ross's teaching of the dual nature of abdominal pain; but while accepting Ross's visceral pain he had suggested that the referred pain and the associated muscular rigidity, so far as the peritoneal cavity was concerned, were due to irritation of the parietal peritoneum. This conclusion was based largely on the clinical phenomena observed in cases of acute appendicitis. Recent injection experiments had confirmed the accuracy of these views. The initial visceral pain in acute appendicitis was transmitted through the splanchnic nerves but the second or localized pain was peritoneal. Pain in the shoulder-tip area felt on stimulating the phrenic nerve terminals in the diaphragm was a striking special instance of the radiation of pain from the parietal peritoneum, and, like the superficial pain in the right iliac fossa in appendicitis, could be modified by subcutaneous injections inducing analgesia of the area of referred pain.

The work of Lewis and Kellgren on referred pain was reviewed. Although Lewis claimed that there was no essential difference between deep somatic and visceral pain, his own experiments failed to produce any reflex contraction of the cat's rectus abdominis muscle on stimulating the gastro-intestinal tract. The method used by Bentley and Smithwick to produce visceral pain by inflating a balloon in the jejunum before and after splanchnic neurectomy for hypertension was described. The afferent nerve fibres from the gastro-intestinal tract ran through the splanchnic nerves on their way to the cord, but they could not properly be described as sympathetic nerves. Recent studies by Bentley and by Bonney and Pickering had suggested that the inflammatory change associated with a peptic ulcer endowed the affected area of the stomach with a tenderness on direct mechanical pressure that was never found in the stomach or duodenum which was not inflamed.

The long controversy on the exact mechanism of the pain in peptic ulcer had ended in establishing belief in the direct effect of hydrochloric acid acting on exposed nerve endings in the ulcer as the true explanation. Recent work on the anaemic zones of skin described by Wernöe as accompanying areas of referred pain had cast grave doubts on the occurrence of these zones. The bearing of cardiac pain on the general problem of visceral pain was discussed; Chester M. Jones and Henry Cohen had suggested a theory of summation of stimuli from both visceral and somatic sources as the most probable explanation of the phenomena of referred pain. Although they had tended to ignore the temporal factor in the summation of pain impulses, some such hypothesis would probably displace the time-honoured theory of an "irritable focus" in the cord.

Correspondence

Strength of the Profession

SIR,—The cumulative effect of the various plebiscites suggests some parallels and comparisons with the N.H.I. struggle which seem to me worthy of consideration. In 1912 we held no plebiscites of the whole profession, for only the general practitioners were directly involved, but we took a great deal of trouble to ascertain what they were prepared to do and the end result was not flattering to our efforts. If we had had then the clear indications which the recent plebiscite gives we might have been spared the humiliation which followed the declaration in December, 1912, that the R.B. considered the Act unacceptable, derogatory, and unworkable. On that day as Medical Secretary I had in my possession a flood of letters and telegrams from Divisional secretaries all over the country which told me that the local doctors were flocking to the panel because they had come to the conclusion that the concessions gained by the Association made it well worth their while to do so. The Meeting, influenced by some eloquent "diehards," refused to hear this evidence. Within a week requests for a Special Meeting came in from many Divisions. The meeting was held, and the resolution rescinded—too late to prevent the Association from appearing foolish and inconsistent. Is history to repeat itself? It should not do so, because the latest plebiscite shows that already a very considerable number of doctors have come to the conclusion either that it will be worth their while to join or that they cannot afford not to do so.

An interesting parallel is that in 1912 the Press and our chief opponents, the Approved Societies, told us we had won a great victory, but we preferred to concentrate on the comparatively minor points we had failed to achieve. The *Westminster Gazette* said: "We all admire the man who does not know when he is beaten. The trouble with the B.M.A. is that it does not know when it has won." In the *Economist* of April 24, 1948, I read the following words which reflect a considerable body of Press and public opinion: "Undoubtedly the doctors have won a big victory, for Mr. Bevan does not easily climb down to the extent that he has done."

I do not think we have won a big victory, because we have failed to hold what to my mind would be the chief security against a whole-time salaried service—namely, the right of private property in the goodwill of medical practices. But we have wrung out the concession that this will not be introduced by Regulation or without a new Act of Parliament. But if the Labour Party should be returned to power at the next election they will be greatly tempted to carry out their declared policy, and in my opinion the best way of preventing this is to use the interval for providing such a satisfactory service that the public would be against any attempt to unsettle the profession once more.

In my opinion—and I say it with regret—to continue to oppose the working of the Service because we have failed on the goodwill issue would be to fly in the face of what is possible. I have three reasons for saying this: (1) we should not have behind us the number of general practitioners we have declared to be necessary for the continuation of opposition; (2) we have no friends for this principle in any of the political parties, and precious few if any in the Press; (3) and, to my mind conclusive, there is a very considerable number of general practitioners who (to my amazement) do not think it is a thing worth fighting for.

As an old medical politician, loving a good fight, I have never seen any good in refusing to face facts and in continuing to try to get the unattainable. I believe our best policy is to accept the verdict of the plebiscite ungrudgingly and to assure those doctors who join the Service that they will have the whole-hearted support of the Association in making the Service a credit to the profession. If we accept this policy much remains to be done, and time is short. The Regulations under which doctors will work must be examined, bringing to bear the unique Regulation-making experience gained in over 30 years of N.H.I. And this experience will be equally valuable to the consultants and specialists who have no similar experience but

will also have to work under Regulations. And of course those doctors who choose to stay outside the Service must be assured of the help of the Association. Vigilance will be needed to ensure that neither they nor their patients will be penalized for their independence.

There never was a time when a strong Association was more necessary, not only for the protection of the doctor but for that of his patients. The great power and prestige earned by our Association during the past few years must not be frittered away, and I think that having proved that we can put up a good fight, and not abandoning our arms, we can do our best work now in the constructional field.—I am, etc.,

London, S.W.7. ALFRED COX.

Balanced Statement

SIR,—To anybody who has followed the editorials of the *B.M.J.* during the past two months those of the last three issues must be a subject of derision. It is now an open secret that the Council was deeply divided on the question of the Minister's concessions: the minority was a considerable one. If we accept the best possible interpretation of their case we are nevertheless convinced that they must have known that the result of their decision must be disastrous—i.e., that the minority action would bring defeat to the majority. The attitude taken by the majority also deserves condemnation. It is true that Dr. Dain at Shrewsbury spoke in the old familiar style, but his letter (April 24, p. 805) was a confirmation of that "careful and balanced statement issued by the Council." This "balanced" statement, as the majority of the Council knew perfectly well, was bound to confuse the doctors' minds. If, then, this argument is well grounded, both the majority and minority deliberately committed themselves to a course of action which of necessity would deeply divide the profession as they themselves were divided.

What is not so clear is the manner in which the minority has captured editorial policy in the last three issues of the *B.M.J.* No impartial reader could say that these were "well balanced." The words may be this or that, but the horrid smell of appeasement comes up from all of those three articles. The *B.M.J.* is dividing the doctors, and it is doing so deliberately. On the eve of battle no general could maintain the morale of his troops by making a well-balanced statement which reflected the indecision and revolt of a minority of his high-ranking officers. The *B.M.J.* and the B.M.A. up to and including April 10 stimulated and sustained our effort admirably. We had the Independence Fund, all the material, all the organization; groups were formed under their conveners; meetings galore were held. Then the leadership faltered and failed. The half-hearted "balanced statement" took its place—for what good reason? Dr. Dain said at Shrewsbury on April 18: "Those who have studied the matter most do not consider that the doctors would be properly safeguarded by the Minister's proposals." Lord Horder, writing to the *Daily Telegraph* on April 22, said: "The situation so far as concerns the freedom of the doctors . . . remains unchanged. The Minister remains all-powerful." These men were in a majority. Why then the abrogation of leadership?

Was the *Manchester Guardian* almost right on April 16 when it said: "The B.M.A. has to consider its position not only in the current negotiations but as the continuing spokesmen of a large part of the profession. . . . If a good number of doctors are brought by Mr. Bevan's belated concessions to change their minds and enter the Service in any case (as seems probable) while the B.M.A. and the rest stay outside, its present strength would dwindle; if it leads its following solidly into the scheme it keeps its strength and its negotiating power." The way is being well and truly laid for a coming announcement in the *Journal*: "The profession has decided to accept," or "The majority is insufficient to warrant a continuation of the struggle," but though that may be superficially true the hard core of truth will be that by means ever so subtle, "balanced statements" which unbalance the reader and a clever course of tone suggestion in the *Journal*, the doctors were conditioned to betray their own freedom. Will you be good enough, Sir, to tell the doctors—you who have prated so much about freedom and independence—what of these things you have achieved for them? You know very well that you have achieved little worth while. The doctors will be just as much the servants of the State machine as if the B.M.A.'s campaign had never started.—I am, etc.,

Burnley, Lancs. H. SIMPSON,
Public Relations Officer,
Independence Committee.

Special Procedure for Regulations

SIR,—I believe that the vast majority of the profession learned with deep satisfaction that the Chairman of Council, in his speech to the Representative Body on March 17, had declared that "the overall considerations which determined 90% of doctors to record their disapproval of the Act had been that the Minister's power under the Act was absolute," and that "that power would lead to the enslavement of the medical profession, which will come to be controlled in effect by the officers of the Ministry." Precisely the same feeling prompted the resolution passed by the Royal College of Physicians of London on March 22 which asked for a "special procedure," by way of a committee, that would serve as a check on Regulations. How urgent such check is becomes apparent from Sect. 66 of the Act, which empowers the Minister and his successors to determine by Regulations alone "the qualifications, remuneration, and conditions of service" of doctors and dentists and other employees under the Act.

When the Minister on April 7 made his statement in the House offering, in response to a request by the Royal College of Physicians, "to make it clearly impossible to institute a full-time salaried service by Regulation alone," I asked him if he would also take into consideration the second resolution passed by the College, asking for a "special procedure" committee. The Minister promised to do so. In his subsequent written answer to the B.M.A., which had endorsed the College resolution, the Minister declared that there is such a committee in operation, but he did not name it.

I am informed by the Table Office, and independently by the Lord Chancellor, that the Committee indicated is the "Statutory Instruments Committee," established by Parliament in 1944. The present chairman of that committee, in a letter (dated May 6) which lies before me, declares that its function "is to inquire only into the technical correctness of Regulations, and not into their merits." It is thus obvious that it would be wholly unfitted to perform the duties desired by the resolution cited. I submit that the demand for effective fulfilment of the request made by the resolution should be fully met in the Amending Act.—I am, etc.,

House of Commons. E. GRAHAM-LITTLE.

Representation of Consultants and Specialists

SIR,—It is clear that there is widespread anxiety among consultants and specialists as to the most suitable body which should represent their views and interests. There is at present a choice between the Royal Colleges, the B.M.A. Consultants and Specialists Committee, the Association of Major (Non-undergraduate Teaching) Voluntary Hospitals, the London Consultants Committee, etc., and now we have proposals, on the one hand, from the British Medical Association for new central and regional consultants and specialists committees elected along democratic lines, and, on the other hand, from the leader writer of the *Lancet*, a new body based largely upon the Royal Colleges and teaching hospitals, with no evidence of a democratic constitution.

Under these circumstances, and particularly in view of the present emergency, the undersigned members of this hospital strongly support the immediate formation by the British Medical Association of new central and regional consultants and specialists committees, provided that they consist solely of consultants and specialists, with an independent secretariat, that their decisions should not be subject to being overruled by the Representative Body, and that these should be taken as being the policy of the Association in matters relating solely to consultants and specialists.—We are, etc.,

C. HEYGATE VERNON,
Chairman, Medical Council, Royal Victoria and West Hants Hospital, Bournemouth.
N. F. ADENEY,
Vice-Chairman.
C. E. P. MARKBY,
Hon. Secretary.

Bournemouth.

Right to Own Practice

SIR,—I am horrified and most disappointed by the tone of your leader in the *Journal* of April 17 (p. 737). The Minister of Health has consistently vilified and abused the medical profession since he first introduced his Bill. There are very many doctors who are in no way committed to, or in favour of, a comprehensive medical service, which is entirely a political movement with a Communist or State capitalism basis. If it was ever suggested by the B.M.A., it is so much the worse. I do not recollect that such a matter ever came to my notice as a member of the B.M.A. for over twenty years. The sole guarantee of freedom for any doctor is the right to own his own practice and to buy and sell as required. This right is recognized in any community which is not based on ideas of State capitalism, and if we give in on this point we cease to be independent individuals but automatically become State servants working on Government premises for a Government salary. Capitation rates are only a salary in a disguised form. It has been often said that the politicians would be more than a match for the doctors, and if the B.M.A. accepts the Minister's proposals at their face value our Negotiating Committee has let us down.

Why all this anxiety to obtain a good press? The general public in this area are almost entirely against this State service, which is entirely politically inspired for the purpose of controlling doctors and public alike. I sent my contribution of £100 as advised as a means to winning our fight for freedom, not in the expectation that the B.M.A. would let down the doctors, and if we give in to the Minister now on account of his transparent and miserable concessions I shall be sadly disillusioned. There is no Government with any support from any part of the population except the Communists who could advocate the confiscation of my practice for a paltry 2½% per annum on its computed value, and any man or any association who permits this to happen is guilty of a completely immoral and illegal act. Before any plebiscite is taken full time must be allowed to discuss this latest attempt to put the State above the individual, and to degrade our country still further by nationalization for nationalization's sake. Once the medical profession goes down, the rest of the country will follow and we shall have lost a glorious opportunity of proving to the world that this country is not in favour of State capitalism. If we accept this Act, we are betraying the entire country.—I am, etc.,

Kirriemuir, Angus. J. MCINTOSH RATTRAY.

Towards a Whole-time Salaried Service

SIR,—For a long time, especially during the last few years, we have been concerned in endeavouring to maintain the freedom of medicine and of its practitioners. To that end we have enunciated certain principles which have been approved and, up to now, adhered to by a practically unanimous profession. I do not intend to try to assess the relative importance of these principles or conditions; I will deal with one which, although mainly concerning general practitioners, cannot but be of importance to the whole profession. This is the question of the right of doctors to retain the ownership of their practices. For brevity, and I hope for clarity, I will speak only on its effect on the maintenance of freedom and independence.

Many of us are greatly concerned that this principle appears to have dropped somewhat into the background and that a number, perhaps a large number, of doctors consider that the Minister has met our requirements. If the profession agrees to surrender this principle, it is difficult, if not impossible, to see how our freedom or independence can be maintained even during the next few years and still more difficult to imagine how further attacks can be repelled in the future. This Socialist Government is committed to endeavouring to promote a whole-time salaried State service, and it is only the strongest pressure (the February plebiscite) which has made it decide that "the time is not ripe" and that its effort must be postponed to a more opportune time. Fresh attacks will be made at a future date by another Socialist Government or by one that is not predominantly Socialist, for we must remember that the present Act really dates back to a Coalition Government. In any case we can expect no support for our contentions from any form of Government if we consider the widespread feeling against us on this matter in all parts of the House.

How can we hope to meet a proposed whole-time salaried State service when it is next launched if we have already sold our practices to the State? Consideration of the fact that medicine has continuously progressed in its beneficent work during many centuries, and that Governments and Ministers are ephemeral in their frets and fumes, ought to be a salutary thought for those on both sides of this controversy and a help to due perspective.—I am, etc.,

Sherborne, Dorset. THOMAS MCCARTHY.

Fix Remuneration

SIR,—In a circular recently received from the London Executive Committee paragraph 3 states that payments to doctors will be made "out of a central pool . . . to be adjusted at the end of two years." There are first charges to be paid from this pool as well as from the amount paid to each individual Executive Council before the doctors can be paid. No *per capita* sum is mentioned. No Spens Committee recommendation is quoted. The doctors are to be remunerated out of the balance, whatever that may be, and even that is subject to revision.

When Lloyd George's National Health Insurance Act came into force the doctors were paid, I think, quoting from memory, 13s. 6d. This was reduced to 8s. 6d. and increased to 10s. by Regulation. Are we to have the same juggling again? The agreed *per capita* fee should be fixed by an Act of Parliament and not reduced by the act of a Minister.—I am, etc.,

London, W.2. R. GALWAY MURRAY.

Alternative Service Suggested

SIR,—The long-drawn-out controversy between the present Minister of Health and the medical profession is becoming increasingly distasteful to everybody, and not least to the doctors, who are being distracted from their work of healing by the exigencies of a bitter political conflict which is none of their seeking. Mr. Bevan has manœuvred himself into a position from which it must be very difficult for him to retreat, though he can hardly blame anyone but himself for this. Is it too much to hope that even at this late hour he might prove himself to be a great statesman by setting aside party considerations and political bitterness, and by approaching the medical profession with the request that they should outline to him their ideas upon the best ways of improving the medical services of the nation?

In South Africa the profession were approached in this way, and were invited to elect a committee to draw up a plan for a national medical service. When a scheme had been produced and was approved by the profession as a whole, the Union Government, after careful examination, found it good, accepted it—and appointed the chairman of the committee Minister of Health. It sounds simple, does it not? But it was statesmanship of a high order—the sort of sound political common sense which has come to be associated with the name of Smuts.

It has long been the concern of the medical profession in Great Britain to ensure that nobody here should go short of the best kind of medical attention because of lack of means, but it has also been their concern that no rigid system should be clamped down upon the people of the country by compulsion and maintained by the threat of legal sanctions. Such a thing is utterly alien to the British way of life.

May I briefly outline a scheme which would, I am sure, meet with the approval both of the great British public and of the medical profession?

(1) The organization of hospital services over natural hospital areas centred on universities, so that these foci of research and education could influence the whole service.

(2) The extension of National Health Insurance benefit to include, as of right, specialist and consultant services (domiciliary when necessary), diagnostic and pathological facilities, physiotherapy, and other treatment in hospitals and nursing-homes.

(3) When this had been effected and was in *efficient* operation, the scope of National Health Insurance to be extended to include the wives, children, and dependants of insured patients and of all of like economic status. Here it might be useful to consider raising somewhat the present income limit for admission to National Health Insurance, and, coupled with this, there should be an agreed scheme to allow "contracting out" for those who wish it—a scheme for grants in aid, for voluntary contributors, etc.

(4) *Experimental* health centres, as became possible, to be set up in suitable areas, and their functioning studied.

(5) A joint advisory body, with freely elected medical members, to be set up to study ways and means of improving and adding to the service as time went on and opportunity offered.

(6) The improved service to be introduced by stages, according to the means and personnel available at the time, and no attempt to be made to introduce at one leap a fully fledged comprehensive service regardless of the existence or otherwise of suitable premises, nursing staff, medical and surgical personnel, and equipment. Indeed, an attempt to do so, as at present proposed by the Government, would result in as much chaos and as disastrous a failure as would have resulted from an attack on Festung Europa launched in 1942 in response to irresponsible demands chalked upon walls to "open the second front now."

Mr. Bevan is intelligent enough to realize full well what chaos will result from an attempt to implement his Health Service Act on July 5, and I believe that he also knows that it will be quite impossible to give a deluded public one tithe of the gifts and benefits he has so rashly promised them. Before it is too late, then, I urge him to think again and so to reap the gratitude of a great nation and the enthusiastic co-operation of a great profession.—I am, etc.,

Wolverhampton. A. VICTOR RUSSELL.

Payment for Work Done

SIR,—I quite agree with Mr. W. Adams, who at our last meeting described the N.H.S. as a gigantic fraud. I for my part will brook no interference between me and my private patients, whom I regard as friends. How would Mr. Bevan like it if I suggested that we reversed matters and undertook to pay each of our patients, say, 20 visits a year—no less and no more—on condition that we drew as much money as we wanted when and how we liked. We might limit it to, say, £10,000 a year. If it is fair one way it is fair the other. My own view is that if we must have a scheme it should be on the lines of the National Deposit Society, whereby the doctor marked down each item and was paid accordingly, so much a visit, etc., by the Society—i.e., paid for work done.—I am, etc.,

Bristol. E. BLAKE GARLAND.

Conflicting Advice

SIR,—Now that the voting is over I would wish to draw attention to one matter which appeared to me unfortunate. Taking the chair at a general meeting of practitioners in my area, among the correspondence there was read out a memorandum sent by a group of members of the Association stating that they were either members of the Council or Representatives, and advising the meeting to vote as they had done before. Whilst agreeing that a Representative has a right to express his own opinion to his constituents, I much regret that certain members of the Council should sign and agree to circulate a document the contents of which did not tally with the advice given by the Council and circulated with the plebiscite papers, unless such publication had been agreed to in Council.—I am, etc.,

London, W.1. PEARSE WILLIAMS.

Doctors' Houses

SIR,—Drs. E. T. Wright and G. H. Rossdale (May 1, p. 855) have indicated serious issues in their letter. I beg leave to elaborate one point—namely, the doctor's house and surgery. As doctors die or retire from general practice the well-known landmarks of long-established doctors' houses will disappear and the populace will have to face ever-shifting doctors' surgeries. This must occur if doctors are obliged to sell their houses by public auction in order to avoid Government legal action for attempting to sell goodwill with their houses. It follows that after July 5 no sensible N.H.S. doctor will buy or build a house with surgery and waiting-room accommodation. No doubt Mr. Bevan in his capacity as Minister of Housing will then produce priorities for G.P.s to become tenants of local authorities and live and work in council houses and prefabs. A doctor will of course need two council houses or two prefabs in order to carry on his practice. Under present circumstances no other course is feasible unless the Government decide to let doctors buy and sell the goodwill of their practices instead of demanding the sole monopoly of this valuable commodity by the State.

It is very probable that Mr. Bevan will in reality be pleased at the prospect of doctors so early becoming the tenants of local authorities and living and working in council houses and prefabs as comrades of the propertyless proletariat. There is little difference between this and the health centre idea, which is primarily to make the doctor's surgery one of many rented from a local authority. The basic idea of the commonplace mind is that the masses are really very stupid and will soon believe that one doctor is just as good as another however much they may at present claim the right to choose their own doctor.

It has been held by the various medical agencies that the prestige of doctors is invariably lowered in the eyes of their patients if they are obliged to live and practice in council houses and prefabs, but as the Government have set themselves irrevocably against the buying and selling of practices this levelling down of general practitioners as a profession must inevitably follow, with disastrous effect on the recruitment of G.P.s to the new Service and the standard of service rendered.—I am, etc.,

Slough, Bucks. N. C. HYPHER.

Appeal to the Courts

SIR,—I am astonished at the decision of the Council of the British Medical Association. We should not willingly accept service under the Health Act unless we can appeal to the courts. If we are treated justly there will be no need to appeal to the courts, but the fact that we are not allowed to appeal to the courts indicates that the Minister of Health intends to treat us unjustly. If he intends to be fair he should be willing to amend the Act to allow appeal to the courts.—I am, etc.,

Liverpool. H. E. ROAF.

Students' International Clinical Congress

SIR,—In July this year an International Clinical Congress of Medical Students—the first of its kind—is to be held in Britain under the auspices of the British Medical Students' Association. Up to date 130 delegates from 30 different countries have accepted our invitation, and a programme of lectures, visits, and ward rounds in various teaching hospitals, discussions, and entertainments for the visitors has been arranged to take place in the Universities of London, Oxford, and Birmingham.

The organizational expenses of the Congress have been met by grants from the British Medical Association and the International Union of Students. The response to invitations so far shows, however, that delegates from many countries are experiencing difficulty in meeting the necessary expense of the attendance. The British Council has generously agreed to cover the Congress fee for a number of delegates, but many countries will have to remain unrepresented unless further support is forthcoming.

May we therefore appeal through your columns for contributions from individual members of the public or from societies which have at heart the furtherance of friendship and understanding of students from all over the world, so that this important event will be truly international in character. Cheques will be gratefully received by the Treasurer, Students' International Clinical Congress, the British Medical Students' Association, B.M.A. House, Tavistock Square, London, W.C.1.—We are, etc.,

JOHN A. RYLE.
Honorary President of the Congress.
STEPHEN DRANCZ.
President of the British Medical Students' Association.
HERBERT E. REISS.
London, W.C.1. Chairman of the Congress Organizing Committee.

Temperature Records and Ovarian Activity

SIR,—Dr. Mary Barton (April 24, p. 806) has not convinced me that I should take rectal rather than oral temperatures. When I use basal temperature records to help me to determine whether a cycle is ovular or non-ovular, the "occasional deceptively low reading due to extraneous factors such as mouth-breathing" is not going to deter me unless she can produce a series of cases in which simultaneous oral and rectal temperatures have been recorded which show that the patients mouth-

breathe so frequently only during the luteal phase that the oral method is unreliable. Should I decide to rely upon basal temperature records to diagnose glandulo-cystic hyperplasia or ovarian cysts, I should require records of the patient's temperature taken over a period of some months before she developed the suspected pathological condition to enable me to determine whether the *absolute* temperature level was of any significance. As for early pregnancy, Dr. Barton still has to prove to me that she demonstrates it more often than I do by my oral temperatures, and the same is true of the drop which occurs when abortion is imminent.

Dr. Barton states that my letter reflects certain common misconceptions concerning the significance of temperature records in the study of infecundity. It is a pity that she did not indicate what those misconceptions are. In my simplicity I employ these records in my Fertility Clinic only to determine whether ovulation takes place, and I should be glad of any evidence she has, based on a detailed analysis of a stated number of cases, that oral temperatures are more unreliable than rectal in this connexion, or that any other infecundity factor may be elucidated by rectal temperatures.

Dr. Barton mentions "thousands of cycles," "several hundred women," "more than 1,500 records gathered from private practice," "observed pregnancies (numbering about 150, and including nearly 90 cases recorded for two months or longer after conception)." She must therefore forgive me if I consider her experience of this subject to be unique. I do, however, believe it to be sufficiently unique to be capable of providing a valuable treatise, based on an analysis of a clearly defined number of cases and/or cycles, which should greatly advance our knowledge of this still controversial subject.—I am, etc.,

London, W.1. P. M. F. BISHOP.

Identification of Medical Documents

SIR,—The article entitled "Identification of Medical Documents" by Prof. Lancelot Hogben and his colleagues (April 3, p. 632) outlines a convenient and relatively simple system of numerical coding which would be a most useful and economical means of patient identification in a punched-card installation. It is doubtful, however, whether the code, employed additionally as a filing instrument, could be conveniently implemented in the majority of our hospitals. Prior to implementing the system it would be necessary to ensure: (1) that there was, in fact, in most hospitals a problem of patient identification that was not completely solved by existing means; and (2) that the code would lead to greater convenience in filing than can be obtained by the present systems.

I would be grateful if you would allow me through the courtesy of your columns to apply these two criteria to Prof. Hogben's code, taking into account also the general procedures for medical documentation at present in operation in our hospitals.

The usual means of patient identification is a card index arranged in alphabetical order, on which are recorded the patient's full name, address, date of birth, employment, and date of admission and discharge, as well as the hospital registration number, which provides the link with the case-notes folder. The largest branch of this hospital has had an alphabetical identifying index of between 200,000–300,000 cards over the course of the past few years, yet there have been very few instances of confusion arising through similarity of surnames, and these have always been satisfactorily solved after additional details have been obtained. The occasions of difficulty have been so few that it is probable that a broadly similar result would have been obtained if Prof. Hogben's code had been employed, since there can be but little doubt that the chances of clerical error are greater in the process of coding than in the mere mechanical process of recording identifying particulars.

Prof. Hogben's code, as he describes it at present, consists of ten digits. This number may well have to be increased so as to provide a reasonable degree of specificity for those areas where there are accumulations of similar christian names and surnames in combination—e.g., the Ian "Macs" of Scotland or the Thomas Jones and John Davies of Wales. If the code is employed as a means of filing case histories, it follows that the filing clerk in her work would have to take into account a number consisting of at least ten digits. This is almost certainly impracticable, since the normal clerk finds it difficult to file correctly when the system entails more than six digits. The normal practice in hospital registration numbering rarely exceeds five digits (except for a prefix to indicate the year) and is always in numerical sequence, which itself minimizes misfiling and is, in addition, a means of checking missing case histories. If this procedure is superseded by Prof. Hogben's code, then it is probable that increased misfiling will follow the increase of the number of factors which the filing clerk has to take into account and the loss of the plain numerical sequence; in addition, a convenient means of checking missing case histories would have to be sacrificed.

Prof. Hogben claims that, following the implementation of his code, reference could be made to the case history without recourse to a "name–address admission-and-discharge register." Case-notes folders are now requested either by name or by diagnosis—the former method being associated with the actual treatment of the patient and the latter with research. If Prof. Hogben's system were adopted (there being no alphabetical identifying index), a busy out-patient sister who has urgently requested case histories by name would also have to be asked to supply, (1) the date of birth, (2) the birth rank, and (3) the maiden name in the case of married women. This she would rightly regard as an unnecessary burden. But the only alternative is an identifying index arranged in alphabetical order on which is recorded Prof. Hogben's code in exactly the same manner as the hospital registration number is recorded to-day.

It is agreed that Prof. Hogben's code would ensure that the medical documents relating to the same individual would be found in the same niche of the filing system in any institution. Within the individual hospital, however, the same result can be achieved provided that the unit system of medical documentation (one case-notes folder for each patient, irrespective of the number of admissions or attendances) is adopted. The fact that, additionally, an individual would have the same filing niche in Beachy Head or Birmingham or Bedford is of little importance provided that the records officer in each locality possesses a well-prepared identifying index, arranged in alphabetical order and linked by means of registration numbers to the case-notes folders.

There is no doubt that Prof. Hogben's code would be of great value in a punched-card installation, but one is forced to the conclusion that, rather than simplifying the internal running of a hospital records system, its effects would be the very reverse. The aim of any hospital filing system must be the speedy accessibility of all case-notes folders; any system which may result in impeding the process should be discarded.—I am, etc.,

RONALD BROWN,
Records Officer.
The Royal Liverpool United Hospital.

Accidental Syphilis

SIR,—Dr. R. R. Willcox is to be congratulated on his interesting résumé of the methods of accidental contamination with syphilis (May 1, p. 850). The list could be carried much further, the methods varying according to the customs of different countries. In North Africa, for example, Lacapère (*La Syphilis Arabe*, Paris, 1923) cites as modes of infection cupping of the nape of the neck, circumcision, tattooing, extraction of teeth, sucking of bites and wounds, common cups, *suçoirs* and *narghilés*, the passing of chewing-gum (Louben) from mouth to mouth, etc. Chancres of the head and even of the pubis may be acquired there at the barber's or from a common razor. The high incidence of accidentally acquired syphilis in infants and young children is an indication of the standard of hygiene in North Africa.

I have had it in mind for some time to write on this subject, but from another angle. Since the war ended there has been a noticeable decay in the art of lying among patients with venereal diseases. In the past, according to the patients, syphilis was often contracted through contact with syphilitic cricket balls, billiard tables, bedposts, bulls' horns, etc. Now my patients seem always to contract their diseases by sexual intercourse.

The lavatory seat was seldom cited, and in the Army it could only be claimed as a cause by officers of the rank of colonel or higher. The last time I heard it mentioned was by a patient with a lip chancre who said, "The only difficulty about this business is that nobody will believe I caught it off a lavatory seat."

If Dr. Willcox is correct in his assumptions, and I—like most patients' wives—will need much more convincing evidence than he has produced, it may be necessary to propound yet another theory for the origin of syphilis which should be named the Haringtonian theory (after Sir John Harington, author of *The Metamorphosis of Ajax*).—I am, etc.,

London, S.W.1. JAMES MARSHALL.

Idiosyncrasy to *d*-Tubocurarine Chloride

SIR,—We have knowledge of a case similar to the first one described in the article on this subject by Drs. T. Cecil Gray and John Halton (April 24, p. 784). We feel that the term "idiosyncrasy" is a misnomer in so far that it does not explain the mechanism operating. Recalling the close analogy between curarization and myasthenia gravis and the great tendency of cases of the latter to respiratory failure, it is reasonable to draw the inference that the action of curare is greater on the intrinsic and extrinsic respiratory musculature than on the rest of the musculature of the body.

Both Prescott and Organe[1] suggest and offer evidence that bronchospasm may occur when intubation is performed in a curarized patient. Prescott also stresses the initial action of curare on the brain stem, which controls vagal activity. As Organe has shown that bronchoscopy in the curarized patient does not predispose to cardiovascular failure, we are then forced to the conclusion that these deaths have their origin within the respiratory system.

The blocking of the normal neuromuscular response at the vagal nerve endings within the bronchi (Hering-Breur reflex) by curare must exert a profound influence on the mechanism of respiration, and is closely analogous to an acute attack of myasthenia gravis, exhibiting similar symptomatology and complications. Even if we do not invoke the hypothesis of a possible bronchospasm, we have to recognize that the passage of tube or bronchoscope into air passages that are in a state of areflexia will not give rise to the expiratory effort associated with normal intubation, and we have no guarantee that the normal mechanism will return in a patient already suffering from some initial degree of respiratory obstruction such as might be caused by a carcinoma of the bronchus.

It is to be noted that the second case quoted by Gray and Halton showed no signs of respiratory obstruction and recovered. We feel therefore that the question of "idiosyncrasy" can be explained on normal physiological grounds. Furthermore, it appears to us debatable whether curare should be used in bronchoscopies if there is any evidence of respiratory obstruction.—We are, etc.,

T. HOWELL HUGHES.
D. HEWSPEAR.

Gloucester.

REFERENCE

1 *Proc. R. Soc. Med.*, 1947, **40**, 593.

Curare and Bronchial Spasm

SIR,—The use of *d*-tubocurarine chloride and thiopentone anaesthesia for bronchoscopy seems to have become a fairly well-recognized method. It has often occurred to me that the combined use in this technique of a drug which depresses the respiratory centre together with a drug which has the capacity to paralyse the respiratory muscles involves considerable danger, as it is impossible to inflate the lungs with oxygen during the procedure and the only alternative, which is to insufflate oxygen through the side tube of the bronchoscope, is far from satisfactory. In addition, most of the patients who are sent to us for bronchoscopy are in poor physical condition and are unlikely to withstand any degree of anoxia. I have used this method for some time without misfortune, but I now feel obliged to give an account of a recent experience.

The patient, a man of 67, was admitted to hospital complaining of lassitude, dyspnoea, and a productive cough. His exercise tolerance was very poor and there was slight orthopnoea. Arteriosclerosis was marked, the heart was considerably enlarged to the left, and the blood pressure was 190/120. There had been some attacks of precordial pain. He was found to have a pleural effusion on the right side and he was running an intermittent pyrexia. A bronchial carcinoma was suspected.

He was given morphine gr. 1/6 (11 mg.) and atropine gr. 1/100 (0.65 mg.) one hour pre-operatively. Pharynx and larynx were sprayed with 2 ml. of 2% amethocaine. A mixture consisting of nikethamide 4 ml., "prostigmin" 5 mg., atropine 1/100 gr., was prepared in one syringe. A No. 8 Magill tube of suitable length was lubricated and an endotracheal connexion fitted, in case of an emergency. A Gordh needle was inserted into a vein and fixed in position. *d*-Tubocurarine chloride, 15 mg., was administered, and this was followed after a three-minute pause by thiopentone, 0.4 g. The respirations were quiet and regular. When the surgeon introduced the laryngoscope a slight spasm of the true vocal cords developed. After a further 0.1 g. thiopentone had been given the bronchoscope was passed easily. All respiratory movement ceased. The thorax was compressed a few times while the surgeon withdrew the bronchoscope from the right main bronchus into the trachea. The pulse volume became weak quite suddenly and slight cyanosis developed. The bronchoscope was withdrawn and a Magill tube passed. No time was wasted during this procedure, but by the time the tube was in position the patient was grey and pulseless, and I have a vivid recollection of a grey pharynx with the cords in the cadaveric position.

The mixture of nikethamide, prostigmin, and atropine was administered easily through the Gordh needle, while continued unsuccessful attempts were made to oxygenate the patient by bag pressure from a Boyle's machine, and I wish to stress the fact that *it was quite impossible to inflate the patient's lungs*. No heart beat could be detected. While an attempt was being made to perform cardiac puncture one inspiratory "twitch" of the diaphragm was seen, and from that moment the lungs could be inflated easily. The pulse returned immediately with good volume, and his colour improved rapidly. The patient's first attempts at spontaneous respiration were in the form of Cheyne-Stokes respiration. He was returned to the ward 55 minutes after the commencement of anaesthesia, and oxygen was administered from a B.L.B. mask. When examined 30 minutes later a left facial palsy was detected, and all the signs of a spastic paraplegia, with increased tendon reflexes, positive Babinski, and clonus on both sides, were evident. A cerebral thrombosis was suspected. Nicotinic acid was administered intravenously and intramuscularly. By evening he had recovered almost completely. The following morning his only complaint, apart from "not feeling too good," was of slight precordial pain. All neurological signs had disappeared. He was discharged from hospital after seven days.

While there were no gross signs of cardiac failure before bronchoscopy, it is obvious from the history that the cardiac reserve was small, and it is likely that there were marked atheromatous changes in the coronary arteries. With the added effect on the myocardium of toxic absorption from the affected lung it is not surprising that a short period of anoxia was sufficient to produce cardiac failure. The cerebral changes were presumably anoxic in origin. It seems certain therefore that the dose of *d*-tubocurarine chloride should have been considerably reduced, or the use of this drug dispensed with altogether. It was, however, surprising and disturbing that even when the patient was in extremis, flaccid and grey, it was impossible to force oxygen into the lungs. I feel certain that I was dealing with a spasm of the smaller bronchioles, as at that stage no striped muscle could possibly have resisted attempts to ventilate the lungs. Whether this hypothetical spasm was due to curare or to thiopentone, or to some other factor, I am not competent to judge.—I am, etc.,

MICHAEL M. BOYLE.

Manchester.

Erythroblastosis and Kernicterus

SIR,—The annotation on erythroblastosis and kernicterus (May 1, p. 843) must not pass without comment lest it be assumed by readers not engaged in this work that the theories there outlined are founded on accepted facts. Surely the annotation is wrong in stating that the staining of nerve cells causes their degeneration. It is generally accepted that the sequence of events is, first, damage to and degeneration of the nerve cells and, secondly, icteric staining of the damaged nerve tissue by circulating pigment; this is entirely analogous to the coloration of cerebral lesions by vital staining in experimental animals.

The hypothesis that the different clinical varieties of haemolytic disease are explicable on the grounds of differences in the quality of the maternal iso-antibodies is not borne out by a study of a large series of cases. In my experience the type of foetal disease cannot be predicted with certainty by determination of the quality of the maternal antibodies. The most that can be said is that a high titre of blocking antibodies is likely to be associated with hydrops foetalis and still-birth. In a recent publication on this subject I gave illustrative case histories in which the lack of correspondence between type of antibody and foetal disease is clearly shown (Cappell, 1947).

Wiener's theory that icterus gravis neonatorum is due solely to anti-Rh agglutinins which are "milked into the foetal circulation in the course of labour" is a piece of arm-chair philosophy which is accepted by no competent pathologist experienced in this work (cf. Potter, 1947). If it were true it would be possible to prevent icterus gravis by caesarean birth

—a possibility unfortunately abundantly refuted by experience. The statement that the changes of icterus gravis are due to agglutinative thrombi in the vessels of liver, bone marrow, and brain is only an attractive speculation which is, unfortunately, divorced from reality and is in direct conflict with all the morbid anatomy of the disease. The post-mortem appearances provide unmistakable evidence of long-continued pre-natal haemolysis, and the extra-medullary haemopoiesis which is so conspicuous a feature of many cases cannot conceivably have developed only after birth.

In conclusion I can only agree with the last sentence of your annotation, but this is just what the American writers cited have failed to do; instead they have promulgated a theory based on pure speculation without a shred of clinical or pathological evidence to support it.—I am, etc.,

The University, Glasgow. D. F. CAPPELL.

REFERENCES

Cappell, D. F. (1947). *Brain*, **70**, 486.
Potter, E. L. (1947). *Rh.* H. K. Lewis, London.

Iridocyclitis Treated with Benadryl

SIR,—I found the letters of Dr. Barbara Shaw (Feb. 7, p. 277) and Dr. J. Moss (Feb. 21, p. 367) on this subject interesting. A patient of mine here, an ex-naval officer, has had recurrent attacks of iridocyclitis for many years and has seen several specialists in addition to many general practitioners.

As the condition always occurred in the right eye only, and dated from his service in submarines during the Kaiser's war, he always referred to it as "periscope eye." I usually relied on atropine and heat, but the various specialists have advised a very varied range of treatment, from arsenicals and pot. iod. to colonic irrigation, prostatic massage, and injections of milk! Last year he had an attack which I treated for a short time with sulphapyridine, but as there was no obvious response I put him on to injections of "acetylarsan" and emetine. This attack lasted for 12 days and was the shortest he had had then.

This month he surprised us all by a fresh attack, but in the left eye for the first time on record, which rather upset the periscope aetiology. I was afraid that occurring in a new eye it might be more severe than before, but I treated it with atropine and hot spoon bathing as before, emetine and acetylarsan, and "benadryl" in addition. This attack is the shortest he has had, and he was clear in nine days this time. I cannot say for certain whether the benadryl actually shortened the time, but its soothing and soporific effect was a great help and the patient appreciated it very much.

The rationale of emetine is that he has suffered in the past from dysentery, and in this colony a great percentage of people sooner or later suffer from chronic amoebiasis and require emetine periodically.—I am, etc.,

Nanyuki, Kenya Colony. G. DUNDERDALE.

Barium Enema and Acute Intussusception

SIR,—Drs. Brenda Morrison and Donald Court are to be congratulated on their excellent account of "Acute Intussusception in Childhood" (April 24, p. 776), but as stated in the annotation (p. 794) "some may differ from them" on their attitude to barium enemata as an aid to diagnosis and as a method of treatment.

As quoted by Morrison and Court, the papers by Nordentoft,[1] Nyborg,[2] and Hipsley[3] show that the barium enema can be of great value both in diagnosis and treatment of *early* acute intussusception.

In two such cases which I saw as surgical registrar at the King George Hospital, Ilford, barium enemata were found to be of value.

Case 1. A well-nourished baby boy, aged 7 months, was admitted 14 to 15 hours after the onset of what seemed to be spasmodic abdominal pain. There was no vomiting, nor was there any blood detected on rectal examination; while the abdomen, though carefully palpated, held no definite lump.

An enema was slowly administered, under anaesthesia, using a very thin mixture of barium; the progress of the barium was followed by viewing with a screen, and the invaginated loop of ileum was clearly seen to "unfold" itself as far as the ileocaecal junction, when the ileum seemed to "jerk" itself back to its normal position. Two days later the child was home, fully recovered.

Case 2. This child was also suspected of having an early (18 hours) acute intussusception, but again the signs were not sufficient to warrant operation. A barium enema confirmed the diagnosis, and also appeared to reduce the intussusception, though no "jerk" was seen. In this case, however, pain and vomiting recurred after a short interval, and at laparotomy an early ileo-caecal intussusception was found. Reduction in the usual way was followed by uneventful recovery.

These cases illustrate how a barium enema can be of value in diagnosis in the *early* stages of intussusception, and when the classic picture is not presented. In Case 1 it was of obvious value as a mode of treatment. Though a failure as treatment in Case 2, the diagnosis was confirmed and no harm resulted.

In this way early cases can be diagnosed, instead of being allowed to become late cases by the "wait and watch" method of observation; whilst in addition to the diagnosis being made the condition may be cured at the same time—thus making operation unnecessary. According to Babcock[4] 60% of intussusceptions are reducible in the first 24 hours by hydrostatic pressure.—I am, etc.,

London, N.W.6. PHILIP HOPKINS.

REFERENCES

[1] *Acta radiol., Stockh.*, 1943, **24**, 484.
[2] *Acta chir. scand.*, Supp. 80, 1943, **89**, 1.
[3] *Surgery*, 1937, **1**, 825.
[4] *Text Book of Surgery*, 1935. W. B. Saunders: Philadelphia and London.

Late News

SIR,—Being a weekly issue, the *Journal* is at times necessarily a week and more behindhand with medical news of importance to members. This delay is added to when the *B.M.J.* is not delivered by post till Monday or even later. And so the daily lay press gets in first with some selected snippet of news which reaches client or patient casually before the doctor to whom in these anxious days it may be of the first importance. What has taken place at Council or R.B. meetings, or at local meetings, or what emanates from a Government department, he gets late, perhaps when already stale.

Members, being widely scattered, depend upon the *Journal* for ungarbled facts for which they have to wait impatiently. In these days, when things move so fast, could not a column or part of one be given in the *Supplement*, whose news looms greater in importance than ever before, in the form of a "Latest News Summary" framed by the publicity department of the Association under the watchful eye of the Editor; this to publish happenings from local as well as Headquarters sources?—I am, etc.,

Bournemouth. S. WATSON SMITH.

Association of Medical Records Officers

SIR,—The need to improve the techniques of medical record keeping has frequently been a subject of discussion, but until comparatively recently little organized action has been taken. Whilst it is recognized that the standard of clinical records is and must remain a medical responsibility, it is thought that this responsibility could be lightened, and medical time and expense saved, by the provision of trained lay assistants. With this end in view an Association of Medical Records Officers has now been inaugurated and it is felt that the medical profession will give their co-operation and guidance whenever it is sought, as they have always done in such matters in the past. Two of the Association's aims are:

(1) To promote the development of techniques in medical record keeping, to diffuse among the members and others all information and technical and general knowledge from time to time available regarding the keeping of medical records or of use in connexion therewith.

(2) To provide opportunities by means of lectures, discussions, or other intercourse among the members for the exchange of information and opinions regarding the method, processes, and technique of medical record keeping.

Training courses for lay personnel already responsible for medical records are being organized in several of the Regions as an interim measure preparatory to a more comprehensive scheme of training. Records officers interested in these training courses and in membership of the Association are invited to get in touch with the honorary secretary.—We are, etc.,

B. BENJAMIN,
Statistician, Public Health Department, London County Council (Chairman of Council).
ELSIE ROYLE,
Records Officer, Christie Hospital and Holt Radium Institute, Wilmslow Road, Manchester, 20 (Hon. Secretary).

POINTS FROM LETTERS

Holiday Patients

Dr. R. LEONARD LEY (Great Yarmouth) writes: I am well aware that neither the Government nor the B.M.A. Council has the time or the knowledge to consider details under the New Health Act. A nice problem has just occurred to me. How are doctors at seaside resorts expected to deal with the doubled populations presented to them during the holiday months?

New Act Necessary

Dr. A. R. EATES (London, S.W.3) writes: . . . Do please demand a holding up of the Act for five years, during which we might be called upon to help the Government to evolve something good, save the nation, and avoid the eternal disgrace of being accessory before the fact of the introduction of a scheme which will certainly fail. A new Act is absolutely necessary.

British Medical Libraries

Mr. ARCHIBALD L. GOODALL (Hon. Librarian, R.F.P.S., Glasgow) writes: I was very interested to read the article of Mr. W. R. Le Fanu on "British Medical Libraries" (April 24, p. 798). I write to call attention to a library which Mr. Le Fanu does not mention—that of the Royal Faculty of Physicians and Surgeons of Glasgow. In its historical section this collection is in many ways unique and worthy of an important place in British medical libraries.

In current periodical literature we subscribe to over 180 journals, including many not easily obtainable elsewhere in Britain. It is available to Fellows of the Royal Faculty, to postgraduate students, and to members of the Royal Medico-Chirurgical Society of Glasgow. In association with the Royal Society of Medicine our collection is available to all research workers, and we have a microfilm reader making the world literature easily reached through the Royal Society of Medicine or the Surgeon-General's Library.

Ambiguity of Act

Dr. J. W. BARNETT (London, S.W.7) writes: . . . We must insist, and keep the B.M.A. up to it, that all amendments (not concessions) proposed by the B.M.A. should be accepted. In addition all clauses of the Act should be further examined and amended to ensure removal of the ingenious and deliberate ambiguity which is such a feature of the Act and allows the Minister full scope to adjust it as and how and when it suits him. Even when all the amendments are accepted, operation of the Act should be postponed till the Minister has provided at least part of the tools for the job—i.e., the extra hospitals, beds, and nursing and domestic staff. Without these essentials the Act must fail in operation, and well the Minister knows it. He also knows that he will have to explain its failure to Parliament and the people. That is easy. He has insulted and antagonized the medical profession and refused all amendments, and of course the wicked doctors who decline to work an unworkable Act will be made the scapegoats. . . .

Penile Carcinoma

Dr. G. P. CHARLEWOOD (Johannesburg) writes: I was interested in Mr. W. Sampson Handley's letter (Dec. 20, 1947, p. 1050) and in the subsequent correspondence. I saw seven cases of carcinoma of the penis in India. In every one the prepuce was loaded with smegma. In none had the patient ever drawn back his prepuce. Circumcision should certainly be performed for those who prefer not to wash. . . .

Representation of Profession

Dr. C. HAROLD WILSON (Sheffield) writes: At a Group meeting in Sheffield recently the recent development in the situation caused by the Minister's offer to introduce an Amending Bill was discussed. Much alarm was caused by Lord Moran's speech in the House of Lords in reply. What authority or right has Lord Moran to say that any reasonable doctor should accept the terms and now co-operate to make the Act a success? Lord Moran, eminent though he may be, does not represent the profession, and particularly the general practitioners. . . . The meeting also expressed the opinion that the Council should be urged to stand out firmly for the retention of the ownership and goodwill of practices. This principle is of far more importance than any of the others, and on this principle the best interests of the patient and the liberty of the doctor depend.

Carbon Monoxide and Cancer

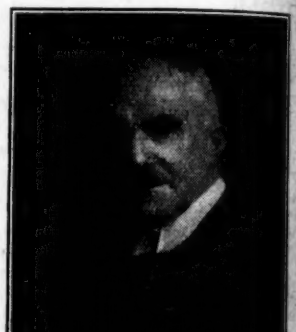
Dr. RICHARD KERRY (Montreal) writes: It is a striking fact that conditions found in cancer—progressive devitalization of red cells, anaemia, exhaustion—would be produced by a focus of carbon monoxide poisoning in the body. If carbon monoxide be the end product of tissue metabolism, and the balance of evidence indicates that it is, it is evident that if growth in any part of the body outstrip adequate blood supply there will be chronic carbon monoxide poisoning, progressive destruction of erythrocytes and exhaustion. . . .

Obituary

PROF. A. H. BURGESS, M.Sc., F.R.C.S., LL.D.

We announce with regret the death of Prof. A. H. Burgess, who was for many years Professor of Clinical Surgery in the University of Manchester. Prof. Burgess died suddenly, at the age of 74, on May 6 in Edinburgh, where he was attending the annual conference of the Association of Surgeons of Great Britain and Ireland, of which he was at one time President. In 1929 he was President of the British Medical Association.

Arthur Henry Burgess was born at Shelford, Lancashire, on Feb. 2, 1874. After leaving school he spent a year in a shipping house in Manchester before entering Owens College, where he graduated B.Sc. in zoology in 1892. In this same year he won the Dauntesey entrance scholarship in medicine and was the Dalton Natural History Prizeman. He was awarded the junior and senior Platt Exhibitions in Physiology in the next two years. Burgess continued with his work in zoology and took the M.Sc. in 1895. A year previously he had also won the Victoria University scholarship in medicine. He took all the medals for class examinations, and concluded his brilliant undergraduate career with the Turner Medical and Dumville Surgical Prizes for 1896, the year when he graduated M.B., Ch.B. with first-class honours. The conjoint examination Burgess took in his stride at the same time. Resident surgical posts in the Manchester Royal Infirmary, the Royal Children's Hospital, and Crumpsall Municipal Hospital followed over the next few years, and he took the F.R.C.S. in 1899. He was then appointed visiting surgeon to the Crumpsall Hospital, and honorary surgeon to the Children's Hospital and to the Christie Cancer Hospital.



[F. W. Schmidt

Burgess introduced modern methods in the practice of surgery in Manchester. He was taught to operate in a long apron with a bib held by tapes round the neck, with rolled-up sleeves and ungloved hands. He adopted at Crumpsall the all-enveloping white overall with a gap only for the eyes. This was such an innovation that a cartoon appeared in the students' *Gazette* showing Dr. E. S. Reynolds, then medical superintendent of the hospital, gazing in mild surprise at this apparition. Burgess was also depicted holding a cystoscope half as long as his own tall self, for he was the first surgeon in the city to become proficient in the use of this instrument. He also gave special attention to intestinal surgery in the days of Murphy's button and Senn's decalcified bone plates, experimenting on the cadaver with various methods applied to a gut which he had dissected out, filled with water, and suspended from a height in order to produce the required pressure. Burgess was one of the early operators for acute appendicitis, and impressed the Manchester Medical Society at one of its meetings in 1907 by showing four specimens that he had removed that day; in each of these cases the appendix was gangrenous. In 1912, in a paper published in the *Journal*, he analysed 500 consecutive cases operated on for acute appendicitis.

Elected honorary assistant surgeon at the Royal Infirmary in 1905, Burgess continued in active work there until 1934, when he retired on reaching the age of 60. His last appearance as a member of the active staff took the form of a clinical round on S5, which was attended by many of his colleagues and a score of his former house-surgeons.

Burgess soon became well known as the leading young surgeon in Lancashire and built up a large consulting and operative practice. Tall and spare in build, he was no dawdler over his work, as the elderly accident-room nurse found when

he became R.S.O. at the Royal Infirmary as successor to one of corpulent build and less active habits. He gave special attention to clinical teaching, carefully preparing beforehand material for his ward classes. There was always competition for the post of house-surgeon on his unit, and many of those who held it became themselves leading surgeons in later life. Burgess had an almost flawless technique, and was careful of every detail in an operation. He was also quick to adopt any new method, such as spinal analgesia and electro-surgery, when it appeared to him to be sound. He trained many junior surgeons in his successful methods and brought great distinction to the surgical school of Manchester. He was very much sought after for addresses at local medical societies, and published several important papers, notably on thyroid and abdominal surgery.

Burgess had joined the Territorial Force in 1908, and during the 1914–18 war he was attached to the large Second Western General Hospital with headquarters in Manchester and took charge of the officers' wards. Later he joined the Thirty-third General Hospital which went to Mesopotamia, where he remained as consulting surgeon to the Expeditionary Force for twelve months. At the Manchester University, after acting as lecturer in surgery, he was elected to the Chair of Clinical Surgery in 1921.

In 1925 Burgess was first elected at the head of the poll to the Council of the Royal College of Surgeons. After ten years as a member of the Council he was made one of its Vice-Presidents. He gave the Bradshaw Lecture on the subject of electro-surgery in 1933. He discussed then with characteristic thoroughness the varieties of heating currents, high-frequency apparatus, effect on tissues, advantages and disadvantages, and the indications for its use. In 1941 Burgess delivered the Hunterian oration, taking as his subject the famous Manchester surgeon Charles White.

When the British Medical Association met in Manchester in 1929 Burgess, as the most prominent and successful graduate of the school, was asked by his colleagues to accept the presidency, and although he did not seek or desire such an honour he accepted the invitation. He attended all the committees in preparation for it, and in the course of the meeting went to bed very late and got up very early to prepare speeches for the various dinners and breakfasts and other occasions. Burgess had a handsome presence and a pleasant voice. A good host and a ready speaker, he made an admirable President. He was elected a Vice-President of the Association in 1931, and for nearly twenty years he served as a member of Council.

In 1930 he went to the meeting of the Association at Manitoba to induct his successor to the presidential chair, and he took part in the proceedings of the Section of Surgery. He received the honorary degree of LL.D. at the University there. Another visit to the United States was in 1931, when Burgess delivered the oration in honour of John B. Murphy before the Clinical Congress of the American College of Surgeons at Chicago, and was elected a Fellow of the American College of Surgeons.

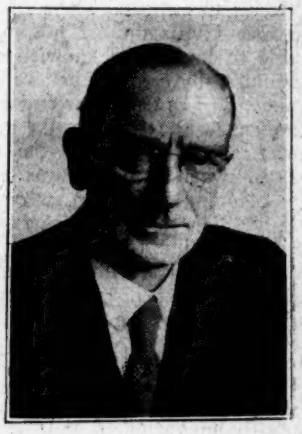
He married Elspeth, the second daughter of Thomas Robinson, of Leek, Staffordshire, and they had four sons and a daughter. His wife died in 1941. The sympathy of his colleagues and many friends will be extended to his family.

Mr. R. L. Newell writes: I was fortunate enough to have been a house-surgeon to Prof. Burgess many years ago, and from that time until his death I have been in close contact with him. In those far-off days I looked up to Prof. Burgess as a great surgeon and a great teacher. I was fascinated by his operative dexterity and his amazing energy, and I held him in very high regard. That conception of him in my youth never altered, though later I counted him amongst my greatest friends and always turned to him for advice, which he so freely gave. His innate modesty made him shy of receiving honours, but one of his particular pleasures was to follow the careers of his many past pupils, and he delighted in any successes that they achieved. I shall sorely miss that upstanding figure—straight as a die—so truly reflective of the great character within.

HARRY STOBIE, F.R.C.S., F.D.S.

We announce with regret the death at Sutton, Surrey, on April 27, at the age of 65, of Prof. Harry Stobie, professor of dental surgery and pathology in the University of London. A student at St. Thomas's Hospital and the Royal Dental Hospital, he took the L.D.S. in 1910, and qualified M.R.C.S., L.R.C.P. a year later.

The loss of Harry Stobie will be felt acutely by the dental profession. He was a lovable character in addition to being an inspiring teacher, with the result that he was held in the highest esteem by all those who came into contact with him. Stobie's name is associated particularly with the Royal Dental Hospital of London, and he was always proud of being a "Royal" man. He was a brilliant student and early showed that he was to leave his mark upon the profession. In the 1914–18 war he was a specialist in maxillo-facial injuries, and at the end of that war, in 1920, he became dean of the Royal Dental Hospital. From that time onwards he devoted a large proportion of his time to dental education, and many of the changes and improvements that have been brought about in the teaching of dental surgery have been due to his influence. He was an examiner in dental surgery for the Royal College of Surgeons, and at various times had been an external examiner for the Universities of Birmingham, Bristol, London, Leeds, and Durham. He had been president of the Metropolitan Branch of the British Dental Association, this being but one of the many positions of honour which he attained. Perhaps the distinction he valued most, however, was that of the honorary Fellowship conferred upon him by the Royal College of Surgeons. He was an excellent teacher and examiner, always patient, always humble, and ever willing to help students to the very utmost of his ability. Few men in the profession have been regarded with such unfeigned respect.



Of recent years he had been in poor health, and those who knew him well were constantly worried when it was clear that at times he was endeavouring to undertake more than he could physically manage. During the last war he was appointed consultant in dental surgery to the Army at home with the rank of brigadier. This appointment was interrupted by illness, and since the war he had never really been a fit man. This did not stop him carrying out his work as professor of dental surgery and pathology at the Royal Dental Hospital, to which post he was appointed in 1939, nor did it stop him attending meetings and committees. It was while Stobie was President of the Odontological Section of the Royal Society of Medicine that he had the rare privilege of being on the Board of Examiners that passed his elder son in his final dental examinations, a fact which gave him great personal pleasure. Stobie gave much of his life to improve dental education. Those students who knew him have happy memories of him as a friend and adviser, and even those who did not have this privilege will feel his influence in their training.

E. GUTTMANN, M.D., M.R.C.P.

D. C. writes: May I add a few words to supplement your obituary notice of Eric Guttmann? By his death psychiatry in Great Britain, and in particular the Maudsley Hospital Medical School, has suffered what can for once genuinely be described as an irreparable loss. His friends, among whom I feel proud to count myself, will always cherish his memory. I have known no man with his ability to grasp the essentials of a problem, whether clinical or administrative, quickly and wisely. For example, I remember most vividly seeking his opinion on the organization of the psychiatric services in the Navy in the early days of the war. After a brief discussion he

produced the next day a scheme which was incomparably more helpful than anything I was able to get from anybody else and which took full cognizance of the special difficulties inherent in naval warfare. It was an astonishing feat of constructive imagination; and one only came fully to realize its wisdom and the accuracy of his predictions with the passage of years. Similarly, your correspondents have indicated his contributions to the organization of Mill Hill E.M.S. Hospital and the Maudsley when it came to be reopened—contributions always made tactfully and without fuss and entirely without any self-seeking or self-advertisement. In both hospitals he was the mainstay of teaching and the dominating influence among his junior colleagues. He was a first-rate clinician, and it is always inspiring to see a first-rate clinician at work.

Eric Guttmann did not parade his great learning but was able to impart his knowledge and ideas so that the recipient could really come to believe that he had thought of the points himself. I can speak as one of the many collaborators to whom he was so generous; in the production of a small textbook for medical students we wrote together. I find myself writing "we," when in fact his was by far the major contribution, both in planning and in execution. He was a very fine man who, in addition to his remarkable intellectual versatility and capacity, was kind, sensitive, witty, pleasantly sardonic, courageous, and loyal. His many friends will, I know, wish to join me in extending our deepest sympathy to his relatives and to his devoted wife. He owed her much.

Dr. ERNEST MAURICE FRAENKEL died on April 20 after a short illness. Dr. Fraenkel was educated at the Universities of Breslau, Munich, and Freiburg. He had been a professor of medicine in the University of Berlin, and was on the staff of the University Clinic, the Charité Hospital, and the Rudolf Virchow Hospital there. Like many other physicians he came to this country in 1932 since it was impossible for him to continue his work in Germany. He was first of all at the Westminster Hospital as a John Prophit research worker. Most of his work at this time was concerned with the Rous sarcoma and with the filtrability of the tubercle bacillus. He took the L.M.S.S.A. in London in 1936, and shortly afterwards was working at the L.C.C. laboratories on the significance of moulds in certain cases of asthma. He was naturalized in 1940, and during the war was in practice in Buxton. On his return to London in 1945 he was made consulting allergist to the L.C.C., and published a number of papers in this and other journals on allergy, bronchial asthma, and related subjects. He was a physician with a philosophic outlook, and some of his ideas were held to be in advance of his time. The sympathy of those who knew him will be extended to his wife and to his daughter.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

The following medical degrees were conferred on May 1:

M.D.—F. Ridehalgh, R. D. Teare, N. Southwell, E. J. Crisp.
M.B., B.CHIR.—*J. C. R. Payne, *R. S. Smylie, *F. S. Mellows, J. L. Hansell, A. I. D. Prentice, R. A. Ryan.
M.B.—*R. D. Ewing.
The title of the degree of M.D. was conferred in April, by diploma, on Mrs. H. E. Dimsdale (Girton College).

* By proxy.

UNIVERSITY OF DUBLIN

The Seventeenth John Mallet Purser Lecture will be delivered by Sir Paul Fildes, O.B.E., M.B., B.Ch., F.R.S., director of the Department of Chemical Bacteriology, Medical Research Council, in the Physiology Theatre of the School of Physic, Trinity College, Dublin, on Tuesday, May 18, at 4.30 p.m. His subject is "Planned Chemotherapy."

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

At a meeting of the Royal Faculty of Physicians and Surgeons of Glasgow held on May 3, with Prof. Geoffrey B. Fleming, President, in the chair, the following were admitted Fellows of Faculty *qua* physician: K. Blum, J. M. Cook, K.-Ul-W. Hazratji. The following were admitted Fellows of Faculty *qua* surgeon: A. J. Leonsins, E. L. F. McConnachie, I. Robins.

Medical Notes in Parliament

NATIONAL HEALTH SERVICE

On April 29 Mr. GAMMANS inquired why the public was asked to choose their doctors now under the National Health Scheme although it would not be known until July 5 which doctors had decided to enter the scheme.

Mr. BEVAN answered that the full list of doctors entering the scheme would not be known until July 5, but some were already entering. In any case doctors' lists of patients should be made up before the scheme started so that individual doctors could settle for whom they would be responsible and might be remunerated for the full number from the start, and so that patients might have a doctor ready to look after them.

On April 29 Mr. LINSTEAD asked when the arbitration Regulations under Section 9 (8) of the National Health Service Act, 1946, would be made.

Mr. BEVAN replied that the National Health Service (Apportionment and Transfer) Regulations, 1948, were made on April 27. These Regulations included a provision for arbitration in respect of disputed transfers under Section 9 (8) of the National Health Service Act, 1946.

Sir ERNEST GRAHAM-LITTLE asked on April 27 what would be the position as regards penalties, by fine or otherwise, of insurable persons who declined to register under the new Act and preferred to continue to receive medical attention from independent doctors; what would be the position of persons who, having registered, found that health services specified under the Act were not provided in the area in which they lived, and whether such persons would be called upon to pay for services which they could not enjoy.

Mr. BEVAN answered that the new Health Service was not based on insurability, and anyone could use it or not, as they wished, at any time. What was available in each area at any time would depend on resources, but—as the great part of the cost of the Service was from taxes and rates—people could not be paying for something that was not available.

On April 26 Sir HENRY MORRIS-JONES asked what guidance Mr. Bevan gave to allocation committees which were to be set up under the National Health Service Act in regard to all persons who were entitled to medical treatment but who had not selected a doctor and might not wish to avail themselves of treatment as insured persons.

Mr. BEVAN replied that the benefits of the National Health Service were not dependent on insurance qualifications. Allocation Committees would deal only with persons who asked to be allocated. A model scheme prepared for the Executive Councils dealt with this matter.

On April 29 Mr. WATKINS suggested that the Minister of Health should make arrangements with the Central Office of Information to offer the services of speakers to organizations and bodies who required information about the provisions of the National Health Service Act.

Mr. BEVAN promised to consider this suggestion, but hoped that those actually engaged in the new Service, such as members of Regional Hospital Boards, Executive Councils, and Local Health Authorities, would be willing to help in this way locally.

Sir ERNEST GRAHAM-LITTLE asked on April 29 how many local authorities had, since Jan. 14, submitted plans for alternative accommodation to replace health centres, whose provision was indefinitely postponed by Circular No. 3, 1948.

Mr. BEVAN repeated his statement of April 15 that Circular 3/48 did not "indefinitely postpone" all provision of health centres. Some local health authorities were already preparing proposals for providing health centres in accordance with the guidance given in the Circular. He did not understand the reference to "alternative accommodation."

Alien Practitioners

Mr. HASTINGS complained on April 29 that doctors covered by Section 3 of the Medical Practitioners and Pharmacists Act, 1947, who had served in Government Departments abroad were still unable to obtain forms of application for registration from the General Medical Council.

Mr. BEVAN replied that the General Medical Council would send the forms to these practitioners almost immediately.

Lady GRANT asked on April 29 whether foreign practitioners serving under the Crown in the Colonial Medical Service were to be allowed to apply for permanent registration under the Medical Practitioners and Pharmacists Act, 1947, although not resident in the United Kingdom.

Mr. BEVAN answered that registration was conditional on residence in the United Kingdom. These practitioners could

ENGLAND AND WALES

A.—Crude Death Rates (all causes) and Case and Death Rates for Chief Notifiable Diseases. Years 1938, 1939, 1945, and 1946

Year	All Causes	Typhoid and Paratyphoid Fever		Cerebrospinal Fever		Scarlet Fever		Whooping-cough		Measles		Diphtheria		Acute Poliomyelitis and Acute Polioencephalitis		Dysentery	
	Death Rate	Case Rate	Death Rate	Case Rate	Death Rate	Case Rate	Death Rate	Case Rate	Death Rate	Case Rate	Death Rate	Case Rate	Death Rate	Case Rate	Death Rate	Case Rate	Death Rate
1938 ..	11·6	·03	·003	·03	·016	2·41	·008	?	·026	?	·037	1·58	·069	·04	·006	·10	·003
1939 ..	12·1	·04	·003	·03	·012	1·88	·004	?	·030	?	·007	1·14	·052	·02	·003	·05	·002
1945 ..	12·6	·01	·001	·05	·014	1·89	·002	1·64	·018	11·67	·019	0·46	·018	·02	·003	·39	·004
1946 ..	12·0	·03	·001	·05	·012	1·38	·001	2·28	·020	3·93	·005	0·29	·011	·02	·003	·19	·003

B. Total Deaths (including Non-civilians) from Respiratory Tuberculosis and Pneumonia

Year	Respiratory Tuberculosis	Pneumonia, all Forms
1938	21,282	27,467
1939	21,542	23,403
1945	20,013	19,984
1946	19,365	20,215

C. Death and Notification Rates per 1,000 total (Live and Still) Births

Year	Puerperal Fever and Pyrexia	
	Case Rate	Death Rate
1938	14·41	0.70
1939	14·48	0·63
1945	10·02	0·24
1946	8·50	0·18

NOTES.—(1) Rates for 1938 are based on civilian and non-civilian data and for 1939, 1945, and 1946, on civilian data only.

(2) Rates for notifiable diseases for 1938 and 1939 are based on original notifications ; those for 1945 and 1946 are based on original notifications corrected for later amendments of diagnosis.

(3) The number of cases of whooping-cough and measles in 1938 and 1939 is not available. Notification of these diseases was not compulsory until 1940.

not be registered under the Act while serving abroad. If they subsequently took up residence it would be open to them to apply.

Deaths from Notifiable Diseases

Mr. SKEFFINGTON-LODGE requested on April 29 figures showing the trends in regard to the death rate and the chief notifiable diseases, compared with the most satisfactory statistics for pre-war years.

In reply Mr. BEVAN furnished the above tables.

Position of Assistants

On May 6 Mr. BOWDEN asked the Minister of Health if a doctor now employed as an assistant could on July 5 commence a separate practice from his principal, providing patients wished to be placed on his panel and the district was not considered to be over-doctored, or must he commence outside of the area in which he was now practising as an assistant ?

Mr. BEVAN said that with the agreement of the Medical Practices Committee an assistant could on or after July 5 practise as a principal in any area under the National Health Service, but the agreement of the Committee would not relieve him from any restrictions imposed by any personal legal agreement previously entered into with his principal.

Doctors' Wives

Sir WALDRON SMITHERS on May 6 asked whether Mr. Bevan had studied details which had been sent him about the position of doctors' wives under the Health Act. Mr. CUTHBERT asked what answer the Minister of Health had given to the request by the League of Doctors' Wives asking him to postpone the introduction of the National Health Act until he had the necessary buildings, equipment, and trained personnel. Sir JOHN MELLOR asked whether Mr. Bevan would provide assistance for those doctors for whom, and for whose households, the National Health Service would cause increased secretarial work, telephone attendance, and aggravate domestic disturbance.

In reply to the three questions Mr. BEVAN said that, as he had told those concerned, he thought there was a tendency to overestimate the effect of the new Service upon the position of doctors' wives. In any case he did not believe that they on reflection would wish to deprive the rest of the community of the benefits of the scheme by postponing the appointed day.

In reply to a further question Mr. BEVAN said that if it was found that extra work was thrown on doctors' wives and they found it burdensome, the Government would consider what help it could give in the provision of domestic service. He reminded Members that there were other wives with onerous burdens as well as doctors' wives.

Cost of the Service

Mr. ODEY on May 6 asked why the new Health Service information leaflet did not state the weekly cost of the stamp contribution. Mr. BEVAN said the National Health Service was not dependent on a stamp contribution, which was a matter for National Insurance.

Mr. ODEY asked for an assurance that Mr. Bevan was not influenced by the fact that much of the new Health Service would not be available for twenty years. Mr. BEVAN said that in every part of the world there must be limitations on health services because of their dependence on the medical and physical resources available. If, as Members asserted, the Ministry would be unable to give the service, then, obviously, there would be no cost. The cost of the service which the Ministry was able to give was borne from the National Exchequer and not from insurance contributions.

Col. STODDART SCOTT asked whether Mr. Bevan said the £200,000,000 which the Health Service would cost was coming entirely from rates and taxes with nothing out of the weekly contributions.

Mr. BEVAN replied that it would come almost entirely from the Exchequer and the rates.

Col. STODDART SCOTT: The right honourable gentleman says "Almost."

DENTAL SERVICES

Sir HUGH LUCAS-TOOTH moved on May 3 that the National Health Service (General Dental Services) Regulations, 1948, dated March 12, be annulled. At the start of the debate Sir Hugh asked that the sitting be suspended owing to the absence of a Minister to reply.

Passing to the Regulations he said that under Subsection 1 of Section 40 in the National Health Service Act, 1946, councils for counties and county boroughs were to arrange with dentists for providing services at a health centre or otherwise. Under Subsection 2 the Minister was to make Regulations carrying out that general intention. The Regulations would deal with the preparation and publication of lists of would-be practitioners in the dental service and would leave it open to every dentist to say whether he wished to come into the scheme. The Regulations were to confer the right on any person to choose his own dentist and to establish a Dental Estimates Board for approving estimates of the cost of treatment. This Section had not been amended in its passage through Parliament.

The White Paper which had been published with the Act stated that dentists would normally be able to start treatment without further reference and subsequently to submit a claim for payment from public funds. Since the Act became law discussion had gone on between the dentists and the Ministry, but there appeared to be a complete breakdown in the negotiations. Two main points were the question of clinical freedom and the question of remuneration. The Minister insisted that the remuneration of dentists should be by fixed fees ; the provisions on the subject in the Regulations were wholly the responsibility of the Minister. At this point Mr. Bevan entered the House.

Proceeding, Sir Hugh said that dentists practising in private surgeries would have to send their estimates to the Dental

Estimates Board. All estimates for dental treatment for the whole country whether requiring prior approval or not had to be sent to a single board of a chairman and eight members. Treatments were divided into those which could be completed without obtaining the approval of the Dental Estimates Board and those requiring prior approval. He was informed that 75% of the work of the dentist fell in the second class. Sir Hugh estimated that in an ordinary practice at least two cases daily would require prior approval. There were twelve thousand practising dentists, so something like 150,000 prior approvals would have to be given weekly.

Blood and Vulcanite

On remuneration the Spens Committee had not yet reported, but the Regulations stated in effect that every dentist would be given a single flat rate for each item of treatment whatever his skill or experience. If a low basic rate was paid without any account for skill, the better dentist would stay out and the only ones who came into the scheme would be those rudely described as the "blood and vulcanite" type. He suggested there should be a classification with a higher rate of charge and the dentists could choose into which classification they went.

Sir WAVELL WAKEFIELD felt there had been discourtesy and there was a strong feeling of dissatisfaction at what had taken place.

Mr. BEVAN said that was the second or third time that the representatives of some part of the medical profession had made this statement. If it was repeated he would publish the verbatim report of the exchanges between him and representatives of the medical profession. All these conversations had been confidential and he was quite helpless when a stupid statement like that of Sir Wavell's was made.

Sir WAVELL WAKEFIELD said he was making a statement of what the dental profession felt.

Mr. BEVAN: It is untrue.

Sir WAVELL WAKEFIELD said Mr. Bevan referred to the medical profession but that he had spoken of the dental profession. He asked Mr. Bevan what were his intentions about dental work which was done by independent qualified dental technicians. He pointed to the provision in the Regulations that as a condition of obtaining general dental services a person should, if required by the Board, submit himself to examination by a dental officer. He thought those words reflected on the professional skill of the dentist. He asked whether members of the Dental Estimates Board would be full-time or part-time members of the Board and for what period they would be appointed.

No Plebiscite

Mr. BAIRD, said the great mass of dentists did not wish to commit themselves until they knew what remuneration they would get. To say that they opposed the scheme was nonsense. Up to the present there had been no plebiscite and no democratic method of judging their views. If there was to be a National Health Service there must be a Dental Estimates Board to adjudicate between patients and dentists and between the Government and the dentists. The great mass of cases would go through the Board without any need for professional opinion at all. The Minister had followed almost word for word the suggestions of the British Dental Association of what should require prior approval. When he himself had suggested that Schedule A should include crowns and inlays, members of the Contact Committee of the Dental Profession turned down the suggestion because they believed some members of the profession were not capable of carrying out all types of crowns and inlays without prior approval. When more skilled work required prior approval by the Dental Estimates Board there could be a varying fee for each item.

Mr. RENTON said the Regulation embodied all the worst fears as to what would happen to a professional service when the Government got hold of it.

Dr. H. B. MORGAN, referring to the Second Schedule, said he could understand that the removal of infected teeth and buried roots could await treatment and reference to the Dental Board, but he was sure that very few fractured jaws could await treatment. It seemed unnecessary to include fractured jaws at all, because very few cases would not receive emergency treatment.

Government Reply

Mr. JOHN EDWARDS, replying to the debate, said the Regulations provided for a high standard of service and Mr. Bevan hoped that the treatment would secure a first-class standard of dental fitness so as to promote general health. He did not expect a dentist to do shoddy work or even what some of them called utility work. The service would be mainly paid for out of taxation, but the Government had sought to reduce to a minimum the intervention of the Dental Estimates Board. There was a striking similarity between the proposals in the Regulations and those advocated by the profession early in 1946. The Minister had indicated his view that in ordinary cases the reply of the Estimates Board would come back within a week. The Board would not see every estimate and pass it. Its job was to supervise a large staff which would deal with these estimates, the majority of which would be capable of being dealt with by means of rules.

He did not know any answer to the problem of special payment for the man who was doing particularly good work and he would be glad to hear further views on the point. Regarding shops for the repair of dentures the Ministry intended that they should not be included in the service. All repairs under the National Health Service would be under the supervision of dentists. It was not the intention of the Government to put any financial limit on expenditure, other than the limits laid down in the Regulations. It desired that whatever was clinically necessary should be done. Dentists had not, at the moment, been asked to join the scheme. The Regulations had been tabled because the Government felt that they should be discussed. The wording of the Second Schedule had been prepared in consultation with the profession. An *x*-ray examination which cost more than two guineas but was urgent would not necessarily have to go to the Dental Estimates Board.

On a Division the Regulations were approved by 147 votes to 45.

Air Ambulances

Answering in the House of Lords on April 27 questions by Lord FAIRFAX OF CAMERON on the provision of air ambulance services from islands off the coast of Great Britain, Lord NATHAN said that at present county councils in Scotland were responsible for air ambulance services but that the Department of Health for Scotland would assume this responsibility on July 5. He was taking steps to secure and extend the provision by British European Airways of adequate ambulance services to islands off the coast of Great Britain. These services, however, depended upon the provision of adequate landing grounds, and that provision was not the responsibility of the Ministry of Civil Aviation but of the health departments or local authorities. Air ambulances were at present available to Islay, Tiree, Barra, Benbecula, Stornoway, Orkneys and Shetlands, South Harris, North Uist, Isle of Man, Scilly Isles, Alderney, Jersey, and Guernsey. Consideration was being given to extension of the service to the islands of Mull, Coll, Colonsay, Fair Isle, and Foula.

British European Airways used D.H. Rapides, which could be quickly converted into air ambulances. The Rapides in Scotland were based on Renfrew and Aberdeen, and those for services off the English coast from bases at Speke, Land's End, and Jersey. In addition the Royal Air Force had two aircraft fitted as air ambulances for the movement of sick Service personnel. These could also be used in emergency to transport civilians. The numbers conveyed from the Scottish islands were 94 cases in 1945; 146 cases in 1946; and in 1947, 168 cases. An air ambulance could be summoned by telephone or telegraph by any doctor whose name was in the list supplied to the British European Airways Corporation by the Department of Health for Scotland. A recent failure to convey two patients from the Island of Westray occurred because the air strip there was insufficient for the safe operation of a D.H. Rapide.

Industrial Injuries.—The National Insurance (Industrial Injuries) Bill which was published on April 30 is designed to forestall difficulties which further study of Section 14 of the National Insurance (Industrial Injuries) Act, 1946, has shown may occur. This section provides a special hardship allowance to an industrial pensioner who by reason of his injury is likely to be permanently unable to return to his old job and for the time being unable to follow employment of an equivalent standard. With recent advances in rehabilitation, doctors may be reluctant to say that a man would never be fit again for his regular occupation. The Bill will therefore authorize the payment of the allowance of 11s. 3d. a week while measures of rehabilitation are being tried.

Overproduction of German Doctors.—Replying on May 3 to Mr. SOMERVILLE HASTINGS, Mr. MAYHEW said certain universities in the British Zone last year offered to take a number of students who claimed to have been refused admission to Berlin University, providing they did not count against the maximum strengths laid down for their medical faculties. The Control Commission could not approve this, as to do so would go directly counter to their policy of preventing the overproduction of men and women for the medical profession, which was already overcrowded. The students must therefore take their chance of acceptance by the Zonal universities in competition with other candidates for places within the permitted strengths of the faculties.

No. 17

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended April 24.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1948					1947 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	43	5	17	1	2	64	8	31	3	—
Deaths		—	1				—	1		
Diphtheria	179	13	42	17	4	175	22	50	25	9
Deaths	1	—	1	—	—	1	—	—	—	—
Dysentery	252	29	16	1	—	61	4	19	—	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	—	—	1	—	—	—	—	1	—	—
Deaths		—					—			
Erysipelas			43	6	2			33	16	1
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				17					19	
Deaths	33	3	6	7	—	72	9	14	5	1
Measles*	9,092	1147	296	117	47	7,962	408	235	46	36
Deaths†			1	1	—	9	1	—	—	—
Ophthalmia neonatorum	52	1	9	1	—	75	8	24	—	—
Deaths										
Paratyphoid fever	3	—	2(B)	—	—	1	—	—	1(A)	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal	593	31	1	6	3	647	43	5	9	5
Deaths (from influenza)‡	10	1	1	2	—	21	5	3	—	—
Pneumonia, primary			192	32				231	25	
Deaths	192	32		13	7		34		16	12
Polio-encephalitis, acute	2	—				1	—			
Deaths							—			
Poliomyelitis, acute	16	2	5	1	—	6	2	—	5	—
Deaths§	2	—					—			
Puerperal fever		—	9		—		1	10		1
Deaths										
Puerperal pyrexia‖	131	14	11	3	—	136	8	11	—	2
Deaths		—					—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,535	113	257	41	35	892	76	150	22	42
Deaths†			—	—	—	—	—	—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	4	1	—	2	—	6	1	—	3	1
Deaths	—	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	3,727	271	55	56	20	2,044	256	322	74	20
Deaths	13	—	—	1	—	15	2	6	3	—
Deaths (0–1 year) Infant mortality rate (per 1,000 live births)	317	36	42	23	10	472	71	65	21	17
Deaths (excluding stillbirths)	4,581	725	621	195	121	4,788	755	574	212	132
Annual death rate (per 1,000 persons living)			12·5	12·2				11·9	13·4	
Live births	8,701	1393	1115	361	272	10,155	1626	1317	444	351
Annual rate per 1,000 persons living			22·5	22·6				26·5	28·0	
Stillbirths	219	26	33			266	33	30		
Rate per 1,000 total births (including stillborn)			29					22		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

EPIDEMIOLOGICAL NOTES

Inoculation against Plague and Typhus in International Quarantine Practice

The World Health Organization Expert Committee on International Epidemic Control decided on April 17 to ask the Executive Secretary of the Interim Commission of W.H.O. to make known to National Health authorities the following: "The Committee strongly emphasized the fact that, whatever its value as a measure of individual protection within the area of a plague epidemic, anti-plague vaccination had no place as a quarantine measure in the international control of the disease"; also "the Committee was strongly of opinion that vaccination against typhus, although it conferred considerable protection to the individual, was not justified as an international quarantine measure." The Committee agreed that the use of insecticides with a residual action should be the chief measure of international action against these diseases.

These views coincide with those expressed on Oct. 16, 1947, by the W.H.O. Expert Committee on Quarantine—views which, endorsed by the Interim Commission, read as follows: "The Committee stressed the fact that inoculation against plague or typhus cannot be required under existing Conventions, and observed that such measures had little value for the protection of countries receiving travellers from infected areas. In its opinion disinsectization of the travellers and their belongings by means of D.D.T. or other efficient insecticides would be more efficacious in preventing the importation of these diseases."

Quarterly Return for England and Wales

The Registrar-General's Quarterly Return for the quarter ended Dec. 31, 1947, was published on May 13. The infant mortality rate was 39 per thousand related live births. This was the lowest rate ever recorded for a fourth quarter in this country, being 4 per thousand below that for the fourth quarter of 1946 and 10 per thousand below the average rate for the fourth quarters of the ten preceding years. The birth rate in England and Wales during this fourth quarter of 1947 was 17.8 per thousand compared with an average rate of 15.2 for the fourth quarters of the five years 1941–5. Stillbirths represented 23.4 per thousand total live and stillbirths, which is 3.4 lower than the rate for the fourth quarter of 1946. The death rate was 11.0 compared with 11.3 for the corresponding quarter of 1946 and an average of 11.8 for the fourth quarters of 1941–5. There were no cases of smallpox notified and no deaths from smallpox registered during the quarter.

Discussion of Table

In *England and Wales* the chief features of the returns were the large rises in the notifications of dysentery 142 and diphtheria 43. An increased incidence was also recorded for scarlet fever 245, while a decrease was reported in the incidence of measles 589 and of whooping-cough 161.

The decline in the notifications of measles occurred mainly in the counties surrounding London; in the north there was an increase. The largest falls were London 213, Essex 76, Middlesex 70, Kent 62; the largest rises were Durham 164, Lancashire 130, Warwickshire 116.

A rise in the incidence of scarlet fever was recorded in most areas except the south-eastern and south-western regions, where a fall of 28 occurred; the largest rises were Lancashire 60 and London 37. The largest variations in the trends of diphtheria were increases of 18 in Lancashire, due to the experience of the county boroughs, and of 12 in Yorkshire West Riding, due to a heightened incidence in the rural districts. The largest changes in the returns of whooping-cough were an increase of 54 in Warwickshire and a decrease of 52 in Lancashire.

A series of fresh outbreaks of dysentery was responsible for the large increase in the notifications of this disease, which reached the highest total for two years. The new outbreaks included Derbyshire, Chesterfield M.B. 68; Sussex, Hastings C.B. 36; London, Kensington 16; Durham, Sedgefield R.D. 12; Middlesex, Tottenham M.B. 11. The other large returns of dysentery were Yorkshire West Riding 39 (Sheffield C.B. 24) and Lancashire 35 (Oldham C.B. 8, Whiston R.D. 8).

In *Scotland* infectious diseases were slightly less prevalent during the week. The largest falls in incidence were dysentery 31, measles 19, and diphtheria 11. The returns for dysentery were the lowest for five months and the total for diphtheria was the lowest for four months.

In *Eire* the notifications of measles rose by 21, while the notifications of whooping-cough fell by 13. The rise in the incidence of measles was fairly general throughout the country, excluding the county boroughs, for which a slight fall was recorded.

In *Northern Ireland* only small variations in the totals of notifications were recorded. The notifications of scarlet fever declined by 11 in the county boroughs but rose by 8 in the remainder of the country.

Week Ending May 1

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,538, whooping-cough 3,684, diphtheria 134, measles 10,169, acute pneumonia 546, cerebrospinal fever 57, acute poliomyelitis 13, dysentery 119, paratyphoid 3, and typhoid 12.

Medical News

Langley Memorial Prize

The Langley Memorial Prize, value £21, is open to competition among officers of the Colonial Medical Service who are serving, or who have served, in West Africa. The prize will be awarded for the best paper submitted on a topic falling within one of the following subjects (special consideration being given to original work): (*a*) tropical medicine or surgery; (*b*) tropical hygiene and sanitation; (*c*) tropical entomology and parasitology. Papers, which may consist of either published or unpublished work, should reach the Assistant Dean, London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1, by Oct. 1.

Oliver Memorial Fund Award

Dr. R. R. Race, director of the Medical Research Council's Blood Group Research Unit, is this year's recipient of the Award of £50 by the Oliver Memorial Fund for Blood Transfusion for his researches into blood groups. The honorary treasurer of the fund (Mr. F. W. Mills, National Provincial Bank, Ltd., Holborn Circus, London, E.C.1) informs us that a similar amount will be awarded next year.

Alleged Cancer Cure

A committee appointed by the Australian Government to inquire into an alleged cure for cancer advocated by Mr. John Braund, a layman of Sydney, has found that it amounts to an outstanding public mischief. The committee said that the treatment included injections of alum, and that in no case it had investigated had Mr. Braund proved his claim that he could cure cancer.

Awards for Cancer Research

The David Anderson-Berry Prizes for 1947 have been awarded to Dr. P. C. Koller, of the Royal Cancer Hospital, London, and Dr. Ralston Paterson, Director of the Holt Radium Institute, Manchester. Prof. Sir William Wright Smith, President of the Royal Society of Edinburgh, presented the prizes on May 3. Dr. Koller's award was for his work on the effect of irradiating tissues with *x* rays, and Dr. Paterson's for his contributions to determining radium dosage.

British Schools Exploring Society

The Northern Quebec Expedition, leaving on Aug. 4 and returning on Sept. 25, needs an honorary physician and an honorary surgeon. Applications are invited for these posts. The entire cost to each member will be £130 plus about £10 10s. for personal equipment. Applicants should apply as soon as possible to the honorary secretary, White Barn, Old Oxted, Surrey, if possible suggesting a day they could come up to London for an interview.

The Almoner

The Hospital Almoners' Association first published a *Year Book* in 1926. In 1940 the *Year Book* was replaced by a small quarterly *News Sheet*. The Institute of Almoners, with which the Association was amalgamated, has now published the first issue of a monthly journal, *The Almoner*. This includes messages from Sir Wilson Jameson and Sir Alfred Howitt, the President of the Institute, together with a number of short articles and a review by Prof. Alan Moncrieff of the interim report of the Royal College of Physicians on certain aspects of social and preventive medicine. The price of the journal is 1s. 6d., and copies may be obtained from the Institute of Almoners at Tavistock House (North), Tavistock Square, London, W.C.1.

N.H.S. Superannuation Scheme

The Ministry of Health has issued a pamphlet entitled "Superannuation Scheme for Those Engaged in the National Health Service" (H.M.S.O. 3d.; free to those in N.H.S.). It is an exposition in simple terms of the superannuation scheme and includes illustrative examples.

Imported Food Amendment Regulations

The Minister of Health and the Minister of Food have jointly made Regulations amending the Public Health (Imported Food) Regulations 1937 to allow the importation of mutton and lamb carcasses from which a lymphatic gland has been removed. The amendment will bring the Regulations into line with present-day practice in exporting countries.

Joint Tuberculosis Council

The main subject considered at the February meeting of the Joint Tuberculosis Council was the action of various Regional Hospital Boards in deputing the overseeing of regional tuberculosis work to medical officers charged with other duties. An instance was mentioned of the appointment of a medical officer in one region to supervise infectious-disease hospitals as well as the tuberculosis service, and also an advertisement for a medical officer whose work would be "mainly concerned" with tuberculosis. The Council felt that the Ministry of Health should have advised Boards to accept and implement the recommendations of the Council published last year, the chief feature of which was the appointment in every region of a regional chest physician, who should have both administrative experience of a high order and clinical ability at specialist level.

Wills

Dr. Brian Arthur McCubbin, of Portsmouth, left £2,997; Captain Bernard Henry Mooring Aldridge, R.A.M.C., £2,092; Dr. George James Rutherford, of Worthing, late Government medical officer in Ceylon, Nigeria, and the Gold Coast, £1,913; and Dr. Maximilian Walter Geffen, of Hampstead, £1,457. Mr. Augustus William Churchill, vice-chairman of J. and A. Churchill, Ltd., medical publishers, left £93,183.

COMING EVENTS

National Society of Children's Nurseries

A conference, convened by the National Society of Children's Nurseries (Norfolk House, Norfolk Street, Strand, London, W.C.2), will be held in the Conference Hall, County Hall, Westminster Bridge, London, S.E., on Friday, May 21, from 10 a.m. to 4.30 p.m. The morning session will be devoted to "The Training and Examination of the Nursery Nurse"; Dr. William Moodie will speak on "the need for training in child care," and Dr. Elizabeth J. Findlay will discuss administrative problems in training the nursery nurse. The general subject for discussion at the afternoon session will be "The Well-being of the Child"; Dr. John D. Kershaw will speak on team-work in child health, Dr. Neil R. Beattie on the care of the whole child, and Miss Mary Darlow on the well-being of Colonial children. Admittance to the conference is free, by ticket obtainable from the secretary of the society at the above address.

Medical Photography

The Medical Group of the Royal Photographic Society will hold its first exhibition of medical photography at the Royal Society of Medicine, 1, Wimpole Street, London, W., from Monday, May 24, to Saturday, May 29.

West London Hospital Medical School

The first Simpson Smith Memorial Lecture will be delivered at the West London Hospital, Hammersmith Road, W., on Thursday, June 10, by Mr. Norman Tanner on "Haematemesis and Melaena: an Investigation of the Place of Surgery in its Treatment."

B.C.G. Congress

The Institut Pasteur will hold the first International B.C.G. Congress in Paris on June 19–23. Topics to be discussed include the experimental study of B.C.G. and its use in human and veterinary practice. Further information may be obtained from: Secrétariat Général du Congrès du B.C.G., Institut Pasteur, 25, Rue du Docteur Roux, Parix XVe.

American Public Health

The 76th annual meeting of the American Public Health Association will take place on Nov. 8–12 at Boston, Massachusetts. Information may be obtained from the Association's Executive Secretary, Dr. R. M. Atwater, 1790, Broadway, New York, 19.

SOCIETIES AND LECTURES

Tuesday

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—May 18, 5 p.m. "*Erythemato-squamous Eruptions*," by Dr. H. J. Wallace.

Wednesday

GLASGOW UNIVERSITY: DEPARTMENT OF OPHTHALMOLOGY.—May 19, 8 p.m. "*Wounds of the Cornea*," by Dr. W. O. G. Taylor.

HARVEIAN SOCIETY OF LONDON.—At 26, Portland Place, London, W., May 19, 8.15 p.m. "*Clinical Research in Medical Education*," by Prof. W. M. Arnott.

Thursday

BRITISH INSTITUTE OF RADIOLOGY.—At Reid-Knox Hall, 32, Welbeck Street, London, W., May 20, 8.30 p.m., *"The Abdominal Emergencies and Use of the Direct Radiograph,"* by Mr. J. N. Young and Dr. J. E. Bannen.

EDINBURGH ROYAL INFIRMARY.—May 20, 4.30 p.m. Honyman Gillespie Lecture: *"The Genesis of Chronic Peptic Ulcer,"* by Prof. Ian Aird.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHARMACOLOGY.—At Physiology Theatre, Gower Street, London, W.C., May 20, 5.15 p.m. *"Enzymes and Drug Action,"* by Mr. J. F. Danielli, Ph.D., D.Sc.

Friday

BRITISH INSTITUTE OF RADIOLOGY.—At Reid-Knox Hall, 32, Welbeck Street, London, W., May 21, 5 p.m. Meeting of medical members; 8 p.m., *"Trends in Therapy Equipment Design,"* by Mr. A. J. Minns and Mr. D. H. Donaldson, M.Sc.

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons, Lincoln's Inn Fields, London, W.C., May 21, 2.15 p.m. Skinner Lecture: *"The Natural History of Malignant Disease,"* by Sir Stanford Cade, F.R.C.S.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS, 58, Queen Anne Street, London, W.—May 21, 5 p.m. William Meredith Fletcher Shaw Memorial Lecture: *"Contracted Pelvis,"* by Prof. J. M. Munro Kerr.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At South Kensington Hotel, 41, Queen's Gate Terrace, London, S.W., May 21, 7.30 for 7.45 p.m. Dinner meeting. Some colour films of plastic surgery from Prof. Kilner's Clinic.

Saturday

NUTRITION SOCIETY.—At London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C., May 22, 10.30 a.m. Open scientific meeting and annual general meeting.

APPOINTMENTS

Robert George Hogarth, C.B.E., F.R.C.S., has been appointed a Deputy Lieutenant for the County of Nottingham.

Leslie George Housden, M.D., has been appointed part-time to the Ministry of Health to advise on the development of schemes for teaching parentcraft.

Dr. Housden qualified in 1923, and proceeded M.D.(Lond.) ten years later. He was awarded the Sir Charles Hastings Clinical Prize in 1932. He has studied and written on mothercraft and child welfare.

BAAR, H. S., M.D., Ph.D., Pathologist, Children's Hospital, Ladywood Road, Birmingham.

HECTOR-JONES, DAVID, M.R.C.S., L.R.C.P., D.M.R.D., Honorary Assistant Radiologist, Hampstead General and North-West London Hospital, Haverstock Hill, N.W.

JEFFERISS, D., B.M., B.Ch., M.R.C.O.G., Assistant Surgeon to Obstetric and Gynaecological Department, Royal Devon and Exeter Hospital, Exeter.

WADE, PHYLLIS, M.B., B.S., D.M.R., Radiotherapist-in-charge, Royal Free Hospital, Gray's Inn Road, London, W.C.1.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Alexander.—On April 29, 1948, to Nancy (née Walmsley), wife of Dr. F. G. Alexander, Birmingham General Dispensary, Small Heath, a sister for David.

Batty.—On May 5, 1948, at Roundhill Nursing Home, Leicester, to Joan, wife of Dr. A. M. Ferens Batty, twin sons.

Ferguson.—On March 31, 1948, at Douglas, to Frances (née Wright), wife of Dr. J. H. Ferguson, a son—Robert Garnett Allen.

Henderson.—On April 30, 1948, at Edinburgh, to Dr. and Mrs. Ian R. Henderson, 10, Milton Drive, Edinburgh, a daughter.

Hovenden.—On April 24, 1948, to Mary (née Powell) and Dr. T. Geoffrey Hovenden, of 99, Church Road, Barnes, S.W., their second child, a daughter—Kate.

Murley.—On May 6, 1948, at 43, Newlands Avenue, Radlett, Herts, to Daphne, wife of Reginald S. Murley, F.R.C.S., a daughter—Jennifer Jane.

Young.—On April 28, 1948, at the Gables Nursing Home, Aylesbury, to Joyce (née Kellow), wife of A. R. C. Young, M.R.C.S. L.R.C.P., Squadron Leader, R.A.F., a son.

MARRIAGE

Kent—Winfield.—On May 4, 1948, H. A. Kent, Captain, R.A.M.C., and Mrs. Kay Winfield, widow of Flying Officer K. B. Winfield.

DEATHS

Beaumont.—On April 23, 1948, at Brandon, Suffolk, Edward Vincent Beaumont, M.B., B.S.

Burgess.—On May 6, 1948, at Edinburgh, Professor Arthur Henry Burgess, M.Sc., F.R.C.S., LL.D., of Ashlea, Cheadle, Cheshire, aged 74.

Chapman.—On May 7, 1948, at Moore Park, Cardross, Katharine Mary Chapman, L.R.C.P.&S.Ed., L.R.F.P.S.Glas.

Davies.—On May 2, 1948, at Carmarthen, Gwylon Davies, M.C., M.R.C.S., L.R.C.P.

Gray.—On May 6, 1948, at Edinburgh, John Alexander Gray, M.B., Ch.B.Ed.

Hayle.—On May 3, 1948, at 25, Liverpool Road, Chester, Geoffrey Hahnemann Hayle, M.B., Ch.B.

Hoare.—On May 4, 1948, at Ditchling, Sussex, Edward Fitzwilliam Hoare, M.D., aged 71.

Raison.—On May 8, 1948, at Queen Elizabeth Hospital, Cyril Alban Raison, M.B., F.R.C.S., of 58, Harborne Road, Edgbaston, Birmingham, aged 56.

Scoones.—On May 5, 1948, at Rosedene, Hythe, Kent, Harold Edward Scoones, M.R.C.S., L.R.C.P.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Convalescent Measles Serum

Q.—*What are the dangers of using convalescent measles serum in a child up to 3 years of age as regards (1) immediate reactions in the nature of serum sickness, (2) remote reactions such as anaphylaxis and rhesus immunization? How can such reactions be guarded against and treated should they occur? Would it not be advisable to give the parents of any child so treated a note to say what had been done so that it could be handed to any doctor who in later years might propose to give the patient any other serum treatment?*

A.—Convalescent measles serum or the more concentrated globulin used for the prophylaxis or attenuation of measles in young children will not cause immediate or more remote reactions like anaphylaxis or serum sickness, because the serum is a homologous and not a foreign protein. The risk of inducing an antibody response in an Rh-negative child (about 15% of the population) will occur only if the whole blood of an Rh-positive person is used. As this last procedure is not common in practice and the risk is a small one there seems little point in "earmarking" any child who receives such treatment.

Desensitization to Sulphonamides

Q.—*Is desensitization to sulphonamides of any value in practice? How long does it last? Does desensitization to one sulphonamide desensitize to other members of the group? What is the best method to use?*

A.—Sensitization to one of the sulphonamides is often specific for that particular drug, and another sulphonamide may be given with impunity. If this is not so, nothing can be done; there is no method of desensitization. If such drugs are withheld for about two years the sensitivity usually disappears spontaneously.

Fouchet's Test

Q.—*What is the technique of Fouchet's test as employed in infective hepatitis and allied conditions? Is this test of value?*

A.—Fouchet's reagent, which is used to detect bilirubin in urine and serum, is:

10% aqueous ferric chloride	10 ml.
Trichloracetic acid	25 g.
Distilled water	100 ml.

For serum, place 1 to 3 drops of serum on a porcelain tile or dish, add an equal volume of reagent, and observe for twenty minutes. If the bilirubin concentration exceeds 2 mg. per 100 ml., a green or blue colour appears, the speed with which the colour develops indicating the concentration of the bilirubin. A few sera give a colour with little more than 1 mg. per 100 ml.

For urine, to about 10 ml. add 5 ml. of 10% aqueous barium chloride, mix and filter. A heavy precipitate should form; if it does not, add a few drops of ammonium or sodium sulphate solution. When all the liquid has passed through, unfold the filter paper and spread it on a piece of blotting paper. Allow one drop of reagent to fall on the precipitate, and observe for about fifteen minutes. A green or blue colour develops if bile pigment is present.

The writer uses the test as a routine method for urine, as it is the most sensitive of all practicable methods. For serum, it is less sensitive than the van den Bergh test and is not quantitative; its value is that it can be used to confirm a diagnosis of jaundice when no laboratory facilities are available. If it is positive in serum and negative in urine the possibility of a haemolytic jaundice should be considered.

Hay-fever due to Ragweed Pollen

Q.—*An American suffering from a severe form of hay-fever chiefly due to ragweed pollen intends to visit Europe (British Isles, France, Switzerland) this summer. He asks whether ragweed grows in these countries, and, if so, which are its months of flowering?*

A.—The ragweeds (*Ambrosia spp.*) are native to North America and exist in Europe only as introductions. Five species have been noted at various times and places in Great Britain as alien or adventitious plants, usually in the neighbourhood of ports. One—namely, Short Ragweed (*A. artemisiaefolia*)—is known to have been established at one time at St. Annes, Lancashire. The same species is reported as having occurred in France, mainly near certain ports, and also at a number of distinct localities in Switzerland. Ragweed pollen is easy to recognize, but only one grain has ever been seen on the thousands of slides the writer has exposed in various places in Great Britain since 1941. Unless an American visitor happened by mischance to walk into a colony of ragweed such as may perhaps exist here and there it is extremely unlikely that he would be exposed to this type of pollen in Europe. The months of flowering in Europe, as in U.S.A., are August, September, and October.

Diluent for Dimethyl Phthalate

Q.—*What simple and easily obtainable solvents should be used for diluting dimethyl phthalate for application to the face and body?*

A.—Dimethyl phthalate can be applied undiluted to the skin without harm. It is probably desirable, however, to use some diluent, especially for persons with sensitive skins. The amount of diluent should not be greater than 60% or the dimethyl phthalate will cease to be satisfactorily effective. Practical tests of certain diluents forming ointments and emulsions are described in a "Report on the Control of Midges," issued by the Department of Health for Scotland (H.M.S.O., 1946, 2d.), and reviewed in an annotation in the *Journal* of April 3 (p. 651). Several of the formulae recommended are now commercially available. One of the most satisfactory is as follows:

Lanette wax ..	5 g.	Oleic acid	27 ml.
Triethanolamine ..	9 ml.	Dimethyl phthalate	100 ml.
	Water 100 ml.		

Treatment of Hirschsprung's Disease

Q.—*What is the best treatment for Hirschsprung's disease in a young boy? Is sympathectomy still thought to give satisfactory results, and, if so, what type of sympathectomy is indicated? Is treatment by spinal anaesthesia alone of any value?*

A.—The pendulum of the treatment for Hirschsprung's disease is probably in process of swinging away from sympathectomy towards various forms of colectomy—in view of the not very satisfactory long-term results of the former. Sympathectomy is, however, still considered the treatment of choice in most centres. The two variations most favoured are: (*a*) bilateral division of the lumbar splanchnics (2–4 in number) or (*b*) arterial sympathectomy of the inferior mesenteric artery. The previously popular presacral neurectomy has been largely abandoned because of its side-effects in producing sterility and also because of its concomitant effect on the rectal musculature. Spinal analgesia alone has been reported by Telford and Simmons (*British Medical Journal*, 1939, **2**, 1224) as giving dramatic and lasting relief. No explanation of this phenomenon has ever been forthcoming.

Neuro-circulatory Asthenia

Q.—*Of late I have seen many cases of neuro-circulatory asthenia in my practice, especially in young married women. Is there any special test to differentiate this condition from the anxiety neuroses; and what is the most effective treatment?*

A.—Neuro-circulatory asthenia, with its many synonyms, such as D.A.H., soldier's heart, and effort syndrome, is now generally held to be a functional nervous disorder. The symptoms of which the patient complains will be seen, on analysis, to be those of anxiety; in the majority an anxiety state is the underlying abnormality, although in some the term "anxiety hysteria" may be preferable. There is thus no distinction to be made between neuro-circulatory asthenia and anxiety neurosis; the first is an anxiety neurosis in which cardiovascular symptoms are more prominent than usual. Effective treatment is as difficult as for other anxiety states. The problem is well discussed by Paul Wood in his Goulstonian Lectures for 1942.

Retropubic Prostatectomy

Q.—*My recent hospital statistics suggest that the public are beginning to appreciate that the modern operation of retropubic prostatectomy is reasonably safe. Such a realization will undoubtedly lead to an earlier seeking of advice by men in their early fifties—a goal towards which we have been aiming. Does this operation produce sterility and/or atrophy of the testes?*

A.—It is doubtful whether the introduction of a new technique of prostatectomy will lead to a much earlier carrying-out of the operation. Attention is drawn to the condition of enlargement only when symptoms of obstruction arise, and these are often delayed until the sixties and seventies. But even if retropubic prostatectomy were eventually to become the operation of choice, it would not materially affect the incidence of post-operative sterility. After enucleation the mechanism of ejaculation is usually destroyed, so that the semen seeps back into the bladder and is passed in the next specimen of urine. The patient is therefore generally sterile, but cases of paternity after prostatectomy are by no means unknown. Atrophy of the testes should not be a sequel of the operation.

NOTES AND COMMENTS

Stability of Penicillin.—Mr. J. RAWLINGS ELLIOTT (Chief Pharmacist, Charing Cross Hospital) writes: In the reply concerning the stability of penicillin ("Any Questions?" April 17, p. 769) I would point out that some of the statements made are not in accordance with usually accepted information. Lamellae and pastilles are supplied in a gelatin base which contains a certain amount of water, and therefore the penicillin in them is liable to undergo hydrolysis and become inactivated. Penicillin creams are actually thick emulsions containing water as the continuous phase, and thus subject to the same decomposition; in fact the N(W)F monograph states clearly that the product must be labelled "Keep in a Cool Place" and "Use Within Seven Days." Lozenges, ointments, tablets, and oily suspensions, on the other hand, are prepared from ingredients free from moisture and may be stored at room temperature for several weeks, or in a refrigerator for a considerably longer period. It is important that the difference in keeping properties of the cream and ointment described in the *Pharmacopoeia* should be recognized if waste is to be avoided.

Exercise in Middle Age.—Dr. NOEL ALDER (Coleshill, near Birmingham) writes: Might I add to the exercises recommended for the middle aged and elderly ("Any Questions?" April 24, p. 816) one which is perhaps the most generally useful, entertaining, and least strenuous—namely, ice skating, especially figure skating? In contrast to walking exercises, which are often boring and even tiring unless taken on level ground, skating, in which friction is reduced to a minimum, requires a much smaller effort whilst training a much greater variety of muscles. In addition to those of the lower limb (extensors, flexors, rotators, ab- and adductors), a skater is constantly using his neck, shoulder, arm, back, and abdominal muscles—the mind being occupied with the fascination of learning or perfecting new figures. Measured rhythmical movements, poise, and balance, which can be acquired without great difficulty, will offer all the benefits of gentle exercise with the least amount of exertion. I can vouch for this from personal experience—I am in my 64th year—and from contact with others who still enjoy skating in the sixth and seventh decades of their lives.

Correction.—Since reporting "The Tragedy of Mount Scopus" (May 1, p. 860) we have learnt that Dr. Dostrovsky was not killed. Dr. Miszurski, the deputy administrator of the Cancer Department of the Hadassah Hospital, was among those killed.

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